CURRENT LITERATURE

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

General and Historical

Abdullaev, A. H. and Sharafiddinov, T. A. Abu Ali Ibn-Sina (Avicenna) on leprosy. Vestn. Dermatol. Venerol. **5** (1981) 76–79. (in Russian)

Having studied the greatest work of Ibn-Sina which made him world-famous, "Canon of Medical Science," the authors put to his credit the description of the etiology, pathogenesis, clinical picture and treatment of leprosy. The great scientist noted correctly that leprosy was a communicable disease and could be contracted by contact with the patient. The air-borne mode of transmission was possible. He attached great importance to such factors as overcrowding of houses, use of the utensils by all family members, etc. Ibn-Sina was among the first to conclude that leprosy control should be based on the isolation of patients from healthy subjects. Studying the manuscripts of dozens of Oriental medical scientists before Ibn-Sina, the authors have not found such a complete description of the clinical picture of leprosy as given by Ibn-Sina. Subsequent studies of Oriental medical scientists could add but little to what Ibn-Sina had said about leprosy. In the authors' opinion, he could be the first to use the term "facies leonina." His recommendations for treatment of leprosy with food rich in vitamins and other means of strengthening the patient have not lost their importance at present.—Authors' Summary

Brennan, P. J. Leprosy vaccine. (Letter to Editor.) Science **216** (1982) 362.

This Letter to the Editor outlines the crucial role of the National Institute of Allergy and Infectious Diseases (NIAID) of the National Institutes of Health in sponsoring basic and applied research on leprosy. Through both grants and contracts, totaling almost $1.5 million annually, NIAID funds research on propagating the causative agent *in vitro*, growing it in armadillos, separating it from infected armadillo tissue, and isolating and characterizing protein and lipid antigens from the purified agent. NIAID also funds studies on the epidemiology, immunology, and serology of leprosy, and coordinates the exchange of materials, such as *Mycobacterium leprae* itself, purified antigens, serum samples from leprosy patients, and polyclonal and monoclonal antibodies. In addition, NIAID administers the U.S.-Japan Cooperative Medical Science Program, wherein scientists from the United States and Japan meet annually to discuss research and progress in several tropical diseases, one of which is leprosy.—(*Adapted from* the Letter to the Editor)

Crawshaw, R. Leprosy—a disease of the heart. JAMA **248** (1982) 573–576.

Dr. Crawshaw is in private practice in Portland, Oregon, U.S.A. He describes, in superb literary style, the profound personal impact of his first encounter with leprosy in Bombay. Dr. Crawshaw visited Dr. Shubhada Pandya at the Acworth Leprosy Hospital and accompanied Dr. R. Ganapati on his rounds in Bombay's Dharavi slums. The candor and emotion portrayed in Dr. Crawshaw's soul searching provide a moving account of the disease touching the heart of a physician—an experience many of us have perhaps shared in times past—and of which it is useful to be reminded.—RCH

Chemotherapy

Balakrishnan, S., Mester, L., Venkataramanaiah, H. N. and Bhatia, V. N. Effect of desoxy fructo-serotonin (DFS) on the multiplication of *M. leprae* in mouse foot pad. Lepr. India **54** (1982) 56–58.

The findings on the effect of desoxy fructo-serotonin (DFS) on the multiplication, in mouse foot pad, of *Mycobacterium leprae* isolated from five cases of lepromatous leprosy including two dapsone-resistant isolates are presented. DFS showed inhibitory effect on all of the three dapsone-sensitive isolates and on one of the two resistant isolates of *M. leprae* studied so far.—Authors' Summary

Bharadwaj, V. P., Sritharan, V., Benkatesan, K., Girdhar, A. and Ramu, G. Vitamin A levels of ichthyotic and non-ichthyotic skin and plasma of leprosy patients with and without clofazimine therapy. Indian J. Med. Res. **75** (1982) 773–777.

Fifty-three cases of lepromatous leprosy who were on clofazimine therapy over varying periods and who eventually developed ichthyosis were studied. Six lepromatous leprosy patients who had ichthyosis but who did not take clofazimine were also included for comparison. Clofazimine and vitamin A levels were estimated in the ichthyotic and non-ichthyotic areas of the skin of these patients; plasma vitamin A levels were also assayed. Clofazimine levels in skin showed an increase with duration of treatment (at least up to 24 months) in both ichthyotic and non-ichthyotic areas. The levels of vitamin A, on the contrary, showed a decrease with increase in concentration of clofazimine. Plasma levels of vitamin A also decreased with increase in duration of treatment with clofazimine, indicating a more possible existence of vitamin A deficiency in these patients. The ichthyotic skin of patients who did not receive clofazimine therapy contained, however, higher levels of vitamin A compared to those on clofazimine therapy. The inverse relationship observed between the skin clofazimine concentration and vitamin A levels calls for further studies.—Authors' Summary

Bourland, J., Van Loo, L. and Pattyn, S. R. Prévalence de la lèpre dapsone résistante au Burundi. Résultats provisoires. Acta Leprol. **86–87** (1982) 29–33.

Les résultats incomplets d'une enquête de dapsone résistance secondaire dans quatre secteurs au Burundi sont présentés. Sur 925 malades multibacillaires 53 étaient suspects cliniquement. En ce moment 38 résultats d'inoculation aux souris sont connus: 28 souches sont résistantes. On peut donc estimer en ce moment que la prévalence de la DDS-R au Burundi se situe aux environs de 4%. Un cas de lèpre DDS-R primaire probable fut confirmé.—Authors' Summary

Chemotherapy of leprosy (Editorial). Lancet **2** (1982) 77–78.

This editorial summarizes the recommendations of the Study Group convened by WHO in Geneva to recommend chemotherapeutic regimens (WHO Technical Report Series No. 675, 1982).

Treatment in both main categories includes once-monthly rifampin, supervised. For paucibacillary cases, rifampin is to be given once monthly in a dose of 600 mg, supervised, together with dapsone (DDS) 100 mg daily, unsupervised; treatment is to continue for six months and then stop. For multibacillary cases, the standard regimen will consist of three drugs—rifampin 600 mg monthly, supervised; DDS 100 mg daily, unsupervised; and clofazimine 300 mg monthly, supervised, with 50 mg daily unsupervised. In some circumstances, this three-drug regimen may be supplemented by the addition of 500 mg ethionamide or prothionamide monthly, supervised, but further studies are needed to assess the contribution of this fourth drug. Where skin pigmentation inherent in the use of clofazimine is totally unacceptable, a possible alternative is ethionamide or prothionamide 250 mg to 375 mg daily, unsupervised. The standard regimen is advised for at least two years in all multibacillary cases, but ideally it should be continued until slit-skin smears are negative. After treatment of this duration, the necessary follow up has not yet

been defined, but a minimum of four years for paucibacillary and eight years for multibacillary patients would be reasonable.—(*Adapted from* the editorial)

Chemotherapy of leprosy for control programmes. WHO Tech. Rept. Ser. **675** (1982).

In its fifth report the WHO Expert Committee on Leprosy that met in 1976 emphasized the need to prevent the much feared development of drug resistance, and, in view of this, recommended that all active cases of multibacillary leprosy (LL, BL and BB in the Ridley-Jopling classification), whether previously untreated or relapsed, should be treated with at least two effective antileprosy drugs. However, relatively few countries and individual centers have introduced multidrug therapy as a routine practice in their leprosy control programs. Furthermore, there has been considerable uncertainty with regard to the selection of appropriate drug regimens for combined chemotherapy, on the grounds of both efficacy and operational feasibility. This is evidenced by the many and various multidrug regimens recommended since 1976.

Welcoming the steady progress made by the Scientific Working Group on the Immunology of Leprosy (IMMLEP) in its long-term objective of developing a leprosy vaccine of proved effectiveness, the Study Group considered that the classical strategy of leprosy control, based on early detection and effective chemotherapy, is likely to remain unchanged for many years. The Study Group reviewed the problem of dapsone resistance (both secondary and primary) which has now become acute. It also reviewed the problem of resistance to other antileprosy drugs and the operational problems that have hindered the implementation of combined chemotherapy.

After reviewing the small number of bactericidal drugs available for the treatment of leprosy, the Study Group proposed certain multidrug regimens to treat the different groups of multibacillary patients, and a further combined regimen designed for the short-term chemotherapy of paucibacillary patients. In addition, the Study Group recommended ways of overcoming the operational problems that might impede the practical application of the proposed regimens in leprosy control programs.—(*From the* Introduction)

Feng, P. C. C., Feneslau, C. C. and Jacobson, R. R. A new urinary metabolite of clofazimine in leprosy patients. Drug Metab. Disposition **10** (1982) 286–288.

Clofazimine is a drug extensively used in the treatment of leprosy. In our initial investigation of its metabolism in humans, we successfully isolated and characterized two metabolites from the urine of leprosy patients. We report now the isolation of a third urinary metabolite from leprosy patients receiving clofazimine treatment. This metabolite was characterized as a hydrated clofazimine glucuronide by mass spectrometry and UV spectroscopy. We propose that it was formed by an initial hydration reaction followed by glucuronidation.

This metabolite is excreted in extremely small amounts in the urine, constituting about 0.2% of the dose (assuming 70% drug absorption). With the two previously identified metabolites, these three compounds are the major colored metabolites of clofazimine in human urine; however, these metabolites account for $<1\%$ of the dose administered to these patients. At these levels one might even suggest that these metabolites are bacterial. However, the metabolite reported here can be synthesized in an *in vitro* system in which UDP-glucuronyltransferase activity is supported in an immobilized mixture of rabbit hepatic microsomal protein.—(*From* the article)

Hardas, U. D. and Jalgaonkar, S. V. PHA-induced blastoid transformation of lymphocytes in leprosy contacts. Lepr. India **54** (1982) 270–274.

PHA-induced blastoid transformation of lymphocytes was studied in 29 contacts of leprosy patients. Twenty-one contacts taking dapsone (DDS) as prophylaxis showed significant depression of lymphocyte transformation, while eight contacts not taking DDS showed no depression as compared to controls. DDS thus has an inhibitory effect on cell-mediated immune response.—Authors' Summary

Janssens, L. Deux case de lèpre paucibacillaire résistants à la dapsone. (Two cases of paucibacillary leprosy resistant to dapsone.) Acta Leprol. **86–87** (1982) 181–183. (in French)

Two patients are presented with a primary resistant BT leprosy. Diagnosis was made on a clinical base: lack of improvement under supervised sulfone treatment and quick regression of the lesions under a short course of rifampin (eight weekly doses). The two children lived together with their lepromatous mothers who are suspected of dapsone (DDS) resistance. Where secondary DDS resistance is found only in multibacillary leprosy, primary resistance shows up in all clinical forms of leprosy.—Author's Summary

Ji Baohung, *et al.* Therapeutic effect of oximes of 3-formylrifamycin SV in the treatment of leprosy. Chin. J. Dermatol. **13** (1980) 205. (in Chinese)

Methyl formylrifamycin [the compound AF-MO of Cricchio, *et al.*, J. Med. Chem. **17** (1974) 396] showed good antimycobacterial activity against 12 strains of mycobacteria *in vitro*, and in experimental murine and human leprosy. Ten lepromatous patients (BL and LL types) were treated with the drug at a dose of 450 mg daily for one year. The therapeutic effect was very close to that of rifampin. Since methyl formylrifamycin contains a simpler radical than the currently used drug, rifampin, the cost in the synthesis of the former would be cheaper than the latter. The authors suggest that methyl formylrifamycin might be considered as a cheaper substitute for rifampin. Methyl formylrifamycin showed certain toxicity to the kidneys. Further toxicological studies are needed.—(*Translation by* Dr. Y. T. Chang)

Kromann, N. P., Vilhelmsen, R. and Stahl, D. The dapsone syndrome. Arch. Dermatol. **118** (1982) 531–532.

Dapsone given in daily doses of 50 mg to 100 mg or greater for as little as two to three weeks can occasionally give rise to a special complex of symptoms. The main components of this dapsone syndrome are high temperature, a maculopapular (morbilliform) rash, lymphadenopathy, and hepatitis. Complete blood cell and WBC differential counts show changes similar to those seen in virus infections, particularly infectious mononucleosis with lymphocytosis and atypical lymphocytes. There is an increase in the number of eosinophils, which presumably indicates an allergic pathogenesis.—(*From* the article)

Kumar, B., Bahadur, B., Broor, S. L., Kaur, S., Gangwar, D. N. and Malik, A. K. Study of toxicity of clofazimine with special reference to structural and functional status of small intestine. Lepr. India **54** (1982) 246–255.

Seventy-eight patients (leprosy—52, vitiligo—26) on long-term oral clofazimine were studied for gastrointestinal and other side effects. Vitiligo patients were given orally 100 mg clofazimine daily for two months and then 100 mg daily for three months. Leprosy patients took 100 mg clofazimine daily for three months. Four ENL patients were given orally 300 mg clofazimine daily in divided doses for six weeks followed by 100 mg daily. Fifteen leprosy patients who had taken the drug continuously for three months and had no prior GI symptoms were taken up for functional and structural intestinal studies. Two patients developed mild diarrhea; two got colicky pain all over the abdomen, and five complained of mild epigastric discomfort. D-xylose test showed mild abnormality in 2 of the 13 patients studied. Total fat excretion was normal in 12 of the 13 subjects, and Schilling's test was normal in all. Of the 14 jejunal biopsies, 9 were normal, 3 had mild, and 2 showed moderate villous atrophy. Clofazimine crystals were seen in the lamina propria in one biopsy under polarized light. In general no correlation was found between the dosage administered, abnormality in mucosal pattern, crystal deposition, and the symptomatology of the patient. Abnormal cutaneous pigmentation was the commonest side effect becoming noticeable after three weeks. Xerosis of the skin of peripheral parts was also a regular feature. Negligible to very light axillary and inguinal staining was seen. No abnormality in any of the eye structures was noted. Discoloration of urine and sweat was noted by

many. No change in color of sputum, hair, or nails was observed.—Authors' Summary

Kumar, B., Narang, A. P. S., Koshy, A., Sharma, S. C. and Kaur, S. In vivo and in vitro drug metabolism in patients with leprosy. Lepr. India **54** (1982) 75–81.

Plasma antipyrine and chloramphenicol clearance was studied in 23 patients with leprosy and 12 control subjects. Drug metabolizing enzymes (aminopyrine N-demethylase and bilirubin UDP-glucuronyl transferase) were estimated in liver biopsy samples of 12 patients and ten controls. A significant decrease in drug clearance and drug metabolizing of enzymes was observed. However, no significant correlation could be obtained between drug half lives and drug metabolizing enzymes or with any of the liver function tests in these patients. The findings indicate that drug metabolism is impaired in leprosy patients.—Authors' Summary

Leprosy in Tamil Nadu. Kusht Vinashak **4** (1982) 12.

Speaking at a news conference in New Delhi at the end of April 1982, the Honorable Dr. H. V. Hande, our Minister of Health, is reported to have said that in the area of leprosy, Tamil Nadu has made good progress. The National Leprosy Control Programme now covers 44,100,000 people in the state, and the number of known cases, at the beginning of 1982, was estimated at 724,000 of which 562,000 cases were under treatment. The prevalence of leprosy has been brought down to 14.03/1000 in 1981, as against 20.4/1000 in 1977. The incidence of leprosy per thousand has also been brought down to 1.4 last year from 2.1 in 1977.

While it is heartening to learn that the prevalence and incidence rates have registered a downward trend in recent years, leprosy workers cannot afford to sit back and rest content. The quality of work at the delivery point requires to be kept up and improved. Hard work and eternal vigilance alone can ensure control—if not eradication—of leprosy in the next two decades.

For too long we have built up hope that sulfones alone would solve the problem of leprosy. Sulfones had two advantages: low cost and easy administration. The initial good results, however, led physicians to overestimate the possibilities of sulfones, and low dosages of the drug were introduced. As one should have expected, low dosage and irregular intake by self-managed patients resulted in resistant strains of bacilli. Today, the mainstays of leprosy treatment are being debated again and, as it occurred in tuberculosis, polychemotherapy has been proposed. Of course, polychemotherapy means more complicated administration, higher rate of side effects and last but not least—a better training of paramedical personnel.

What drugs do we use? And what schedule do we follow? If the schedule is too complicated and expensive, we cannot achieve positive results, and we would be facing problems of resistance to the new drugs.—(*From* the article)

Pattyn, S. R. A comparison of the bactericidal activity of a series of rifampicins against *Mycobacterium leprae*. Arzneim.-Forsch. **32** (1982) 15–17.

The bactericidal activity against *Mycobacterium leprae* of six 3-(4-methylpiperazin-l-yl-iminomethyl)rifamycin SV (rifampin) derivatives was compared with that of rifampin in a modified proportional bactericidal test, using a smaller number of experimental animals and allowing the administration of a single dose of the drugs. No correlation was found between the *in vitro* activity of the rifamycin derivatives against *M. tuberculosis* or rapidly growing mycobacteria *in vitro* and the activity against *M. leprae* in the mouse. The procedure is valuable for the screening against *M. leprae* of very potent bactericidal drugs available in only small quantities.—Author's Summary

Sinha, M. R. Fixed genital drug eruption due to dapsone. Lepr. India **54** (1982) 152–154.

A case of fixed genital drug eruption due to dapsone is reported.—Author's Summary

Smith, W. C. S. Chemotherapy of leprosy (Letter to Editor). Lancet **2** (1982) 490.

This Letter to the Editor objects to the universal implementation of the recommendations of the WHO study group which advocate multi-drug regimens for leprosy [Chemotherapy of Leprosy for Control Programmes, WHO Technical Report Series 675; Chemotherapy of Leprosy. Editorial. Lancet **2** (1982) 77–78]. The author questions how these new drug regimens are to be funded and doubts that these short courses have been well enough evaluated over a long enough period to justify being recommended worldwide. The author points out that the main reason for the present poor performance of dapsone monotherapy (low percentage of all leprosy patients receiving it, irregular treatment, poor attendance, and poor compliance) has been the lack of resources in the countries with a high prevalence of leprosy. The recommended regimens would cost approximately four-times more than the cost of dapsone alone for paucibacillary leprosy, and for multibacillary cases the combination regimens would be about seven-times more expensive. Implementation of these new regimens would require a large injection of funds, and the author questions where these funds are to come from. At present only a minority of of the estimated number of patients with leprosy receive dapsone. If the new regimens were introduced without the necessary funding, then even fewer patients could be treated or the same number given irregular treatment with three drugs instead of one, leading to the development of multiple-drug-resistant organisms. The author feels that the new recommended regimens are only relevant to developed countries which have few cases of leprosy and which have the necessary resources to implement the regimens. If these regimens were implemented in developing countries without a large injection of resources, they could have disastrous consequences with the development of multiple-drug-resistant organisms and the already restricted leprosy services able to treat only few cases.—(*Adapted from* the Letter to the Editor)

Valles, M., Cantarell, C., Fort, J. and Carrera, M. IgA nephropathy in leprosy (Letter to Editor). Arch. Intern. Med. **142** (1982) 1238.

The authors' present a case report of a 47-year-old man with lepromatous leprosy of 30 years duration who was being treated with dapsone (DDS). A renal biopsy was performed and showed deposits of IgA and C3 in a nodular pattern of predominantly mesangial distribution. Additionally, there were IgA deposits in the lumen of renal tubules. This observation adds IgA nephropathy to the list of several types of glomerular disease that can accompany lepromatous leprosy.—(*Adapted from* the Letter to the Editor)

van Rensburg, C. E. J., Gainer, E. M. S., Imkamp, F. M. J. H. and Anderson, R. Effects of clofazimine alone or combined with dapsone on neutrophil and lymphocyte functions in normal individuals and patients with lepromatous leprosy. Antimicrob. Agents Chemother. **21** (1982) 693–697.

The effects of clofazimine on neutrophil activities such as random motility, migration to the leukoattractants endotoxin-activated serum and N-formyl-L-methionyl-L-leucyl-L-phenylalanine phagocytosis of *Candida albicans*, postphagocytic hexose-monophosphate shunt activity, and myeloperoxidase-mediated iodination and the effects of clofazimine on lymphocyte transformation to mitogens were assessed *in vitro* and after ingestion of the drug by normal individuals and patients with lepromatous leprosy. For *in vitro* studies, the concentration range of the drug investigated was 10^{-6} M to 10^{-2} M. For *in vivo* studies, subjects ingested 200 mg of clofazimine daily for a period of five days. At concentrations of 5×10^{-6} M to 5×10^{-3} M clofazimine caused a progressive dose-dependent inhibition of neutrophil motility without detectable effects on phagocytosis, postphagocytic hexose-monophosphate shunt activity, or myeloperoxidase-mediated iodination. Over the same concentration range, clofazimine inhibited lymphocyte transformation. The inhibitory effect on neutrophil motility was associated with a spontaneous stimulation of oxidative metabolism and could be prevented by coincubation of dapsone with clofazimine. After ingestion of clofazimine responsiveness

of lymphocytes to mitogens was decreased in normal volunteers and leprosy patients; neutrophil motility in normal individuals was likewise inhibited.—Authors' Summary

Venkatesan, K., Bharadwaj, V. P., Sritharan, V., Sreevatsa and Girdhar, B. K. Disposition of dapsone in protein deficiency—An experimental study in mice. Lepr. India **54** (1982) 95–99.

With an aim to evaluate the metabolic disposition of dapsone (DDS) in protein malnutrition, a study was undertaken to determine DDS content of blood and tissues of protein deficient mice in comparison to the levels in *ad libitum* and pair-fed mice. Three groups of Rockefeller's strain mice of the same sex (roughly weighing 25 g) were fed on low protein diet and high protein diet (for pair-fed and *ad libitum* groups). After one month feeding, DDS was administered by oral intubation daily for seven days at a dose of 0.02 mg per g body weight. On the seventh day the animals were sacrificed 3 hr after DDS administration. Heparinized blood was collected from ocular plexus. Tissues (liver and kidney) were taken out for DDS estimations. DDS levels were determined by the method of Simpson (1949) and tissue protein content was assayed by the method of Lowry, *et al.* (1951). Hypoproteinemic mice presented higher values for blood and tissue DDS as compared to their pair-fed and *ad libitum* fed groups. Our observations indicate that in hypoproteinemic mice, on account of the possible diminished binding of DDS to plasma albumin, the concentration of free DDS in blood and in tissues is higher.—Authors' Summary

Yawalkar, S. J., McDougall, A. C., Languillon, J., Ghosh, S., Hajra, S. K., Opromolla, D. V. A. and Tonello, C. J. S. Once-monthly rifampicin plus daily dapsone in initial treatment of lepromatous leprosy. Lancet **2** (1982) 1119–1202.

In an international multicenter controlled single-blind trial of 93 previously untreated lepromatous leprosy patients the therapeutic effects of adding rifampin, 450 mg/day orally or 1200 mg once monthly in a single oral dose, to dapsone (50 mg/day orally) for the first six months of treatment were compared. Clinical and histopathological improvements and bacteriological regression, indicated by the decreases in the bacterial and morphological indices of the skin and nose-blow smears, were satisfactory and practically identical after six months' treatment. The once-monthly rifampin schedule was better tolerated than the daily one. In view of the good therapeutic efficacy and tolerability, the much lower cost of treatment (about one-tenth of that of the daily rifampin regimen) and the possibility of administration under supervision, once-monthly rifampin given in a single oral 1200 mg dose should be recommended, along with a standard dapsone regimen, for large-scale, initial, and intensive combination treatment of patients with lepromatous and borderline-lepromatous leprosy, to help prevent an increase in dapsone resistance. A third antileprosy drug (e.g., clofazimine) may be added to this initial dual-treatment regimen.—Authors' Summary

Clinical Sciences

Baji, P. S., Kher, J. R., Ganeriwal, S. K., Reddy, B. V. and Bulakh, P. M. Electrophoretic pattern of proteins in lepromatous leprosy. Lepr. India **54** (1982) 82–94.

Serum total proteins and the various protein fractions were studied in 50 cases of lepromatous leprosy and in 11 cases of lepromatous leprosy with lepra reaction. The study revealed a significant increase in serum total proteins in both lepromatous leprosy and lepra reaction groups, when compared with normal healthy subjects. The percentage rise was found to be 14.5% and 22.95% for lepromatous leprosy and lepra reaction, respectively.

The globulin fraction showed a significant elevation; while albumin showed a de-

crease. Thus a reversal of A/G ratio was observed in both the disease groups.

Alpha-1 and alpha-2 globulins were found to be significantly increased in both the disease groups. Beta globulins did not reveal any significant alteration. It was interesting to note the presence of an additional globulin fraction in 17 patients of lepromatous leprosy and two cases of lepra reaction. Gammaglobulin showed a significant rise in lepromatous leprosy (56.16%) and in lepra reaction (60.72%). The significance of the above findings are discussed in the light of available literature.—Authors' Summary

Bulakh, P. M., Kowale, C. N., Ranade, S. M. and Deshpande, V. A. Serum enzyme profile in tuberculoid leprosy. Lepr. India **54** (1982) 69–74.

Serum enzyme profile was studied in 74 patients with tuberculoid leprosy and compared with that of 100 healthy controls. The enzymes studied were aspartate, alanine transaminase, isocitric dehydrogenase, alkaline phosphatase, choline esterase and creatine kinase. Both transaminase and alkaline phosphatase were in general within normal limits in tuberculoid leprosy. Creatine kinase levels were found to be significantly elevated. In some of these cases raised levels of serum aspartate transaminase was also noticed—evidence for skeletal muscle destruction. Mild increases in isocitric dehydrogenase and a concomitant increase in alanine transaminase in some of the patients suggest a sub-clinical hepatic damage. A statistically significant decrease in serum choline esterase level was noticed in this study on tuberculoid leprosy patients.—Authors' Summary

Cardenas, Z. L., Daniel, A. A., Zangroniz, L. G. and Fiol, L. M. B. Serología para determinar sífilis en pacientes de Hansen en el municipio Plaza de la Revolución durante el año 1977. (Serology to determine syphilis in Hansen's disease patients at Plaza Municipality during 1977.) Rev. Cub. Med. Trop. **33** (1981) 135–140. (in Spanish)

VDRL's were performed in 74 patients with Hansen's disease at Plaza de la Revolución Municipality. The patients had clinical characteristics corresponding to indeterminate, lepromatous, tuberculoid, and dimorphous leprosy. Only five (6.8%) of the serological assays performed were reactive. Three out of the five reactive serologies were seroresistant and the other two were false-positive reactions. In this study, the percent of false-positive reactions in Hansen's disease was 2.7%.—(*Adapted from* the Authors' Summary)

Cook, G. C. Xylose absorption in Papua New Guineans with leprosy. Acta Trop. (Basel) **39** (1982) 91–96.

Blood xylose concentrations were measured at 60, 90, and 120 min after 25 g xylose was given orally in 33 well-nourished Papua New Guinean in-patients at Port Moresby; 12 had lepromatous (group A) and 7 non-lepromatous (group B) leprosy, and 14 were controls (group C). Differences between mean xylose concentrations were not significant at any time interval. Three patients (2 in group A and 1 in group B) had 90 min xylose concentrations <2.0 mmol l^{-1}. There was no association between xylose concentration and current therapy. Leprosy does not impair small-intestinal absorptive function; it therefore differs from other chronic infections, in which there is xylose malabsorption.—Author's Summary

Dabholkar, V. R. and Gaitonde, B. B. A study of autonomic functions in leprosy. Lepr. India **54** (1982) 303–317.

Two groups of leprosy patients were compared with normal individuals for the evaluation of the functional status of the autonomic nervous system, with the aid of several established procedures. Our findings reveal that in the leprosy patients the adrenergic system is hypo-functional as compared to the cholinergic. Further, in the maculoanesthetic group, there appears to be a physiological Dale's vasomotor reversal when adrenaline was used.—Authors' Summary

Dong Li-Wen, *et al.* Type I lepra reaction induced by lepromin test: A case report. Chin. J. Clin. Dermatol. **11** (1982) 145. (in Chinese)

Type 1 lepra reaction has been observed in a borderline tuberculoid (BT) leprosy patient after intradermal injection of 0.1 ml standard Mitsuda lepromin. The patient was quiescent for more than ten years before the lepromin test. Severe acute neuralgia with nerve enlargement of the left lesser occipital, supraorbital and buccal branch of the facial nerve suddenly appeared eight days after the lepromin test and rapidly developed to a partial facial paralysis but without any skin lesion. The reaction was gradually controlled after prednisone treatment. Lepra reaction is rarely induced by lepromin test. Nevertheless, the lepromin test is a 'micro vaccination.' Both in experimental animals and in human beings it has been shown that lepromin has the capacity to induce a delayed type of skin reactivity and also to induce protective immunity against leprosy or tuberculosis in experimental animals, i.e., trigger a T cell response. Probably this patient not only still harbored a few antigens of the leprosy bacillus in or nearby some peripheral nerves in spite of chemotherapy but also had the potential to mount a cell-mediated immune response against a suitable amount of exogenous antigen(s) of the leprosy bacillus. This may be the mechanism of a Type 1 lepra reaction induced by the lepromin test.—Authors' Summary

Farnarier, G., Mouly, A. and Morris-Vidal, D. Les lesions corneennes de la lepre. A propos d'un cas de lepre autochtone. (Corneal changes in leprosy. A report of an autochtonous case.) Med. Trop. (Marseille) **41** (1981) 515–518. (in French)

The patient was affected by a lepromatous leprosy and had a unilateral edema of the posterior layers of the cornea with a conjunctival hyperemia.

The authors review the various aspects of corneal changes in leprosy: paralytic and non-specific changes in trigeminal paralysis; direct and specific changes: opacification of corneal nerves, avascular keratitis, corneal leproma, disorders of the vascularization either by pannus or by interstitial vascularization.

The epidemiological problems are briefly considered—(*From* Trop. Dis. Bull.)

Garcia, R., Salibian, A., Llorente, B., Pacin, A. and Fliess, E. L. Perfil de las isoenzimas de la dehidrogenasa lactica en el suero de pacienteshansenianos. (Lactic dehydrogenase isoenzymes in the sera of hanseniasis patients.) Hansen. Int. **5** (1980) 119–122. (in Portuguese)

The LDH isoenzymes levels in fresh serum of seven patients affected by different forms of hanseniasis from Argentina, were measured by acrylamide electrophoresis. In all cases the LDH-4 fraction was found elevated; on the contrary, LDH-2 was reduced. The LDH-5 fraction was detected in only three serums, all of them significantly increased when compared with controls.—Authors' Summary

Guha, P. K. and Ghosh, M. Progressive lepra reaction. Lepr. India **54** (1982) 149–151.

Although the reactional tendency is fundamental to leprosy, it is important to recognize a progressive lepra reaction, which may be associated with the patients of lepromatous leprosy. Progressive lepra reaction, more often than not, is both serious and chronic, contrary to a simple ENL reaction which is usually episodic and short-lived. A case of progressive lepra reaction has been presented in this paper.—Authors' Summary

Jerath, V. P. and Desai, S. R. Diversities in clinical and histopathological classification of leprosy. Lepr. India **54** (1982) 130–134.

One hundred thirty untreated cases of leprosy were selected and classified clinically and histopathologically according to Ridley and Jopling (1966) to study the correlation between them. Clinically the most common form was tuberculoid in 55 cases. Clinical and histopathological correlation was found in 89/130 cases (68.5%). Most of the diversities were one step up or down in the TT-LL scale.—Authors' Summary

Kannan, K. B., Venkatesan, K., Bharadwaj, V. P., Sritharan, V. and Katoch, K. Indirect assay of beta hydroxy beta methyl glutaryl CoA reductase in the sera of leprosy patients—A further probe into

cholesterol metabolism. Lepr. India **54** (1982) 242–245.

With an aim to study the cholesterol biosynthetic capacity of leprosy patients, the enzyme beta hydroxy methyl glutaryl CoA reductase (HMG CoA) has been indirectly determined in the sera of leprosy patients and their family members by assaying the circulating levels of HMG CoA and mevalonate and finding out the ratio between the two. The ratio was around 1 in leprosy patients, indicating a normal HMG CoA reductase activity, and approximately the same values were obtained in cases of healthy controls. The results suggest that cholesterol biosynthetic capacity of leprosy patients is normal. Whether cholesterol, the final product or intermediates like mevalonate are utilized by the invading *M. leprae*, thereby causing a lowered cholesterol level, remains to be seen.—Authors' Summary

Kapur, T. R. and Verma, R. D. Study of dermatoglyphics in tuberculoid leprosy. Lepr. India **54** (1982) 143–148.

Dermatoglyphics patterns and total ridge count have been studied in 25 cases of tuberculoid leprosy and were compared with 25 controls. There were no statistically significant variations in loops, whorls and total average ridge count. There were four (1.6%) arches in tuberculoid leprosy as compared to 11 (4.4%) of controls, not statistically significant. There was more decrease of arches on the left hand of the patients as compared to the left hand of the controls.—Authors' Summary

Kumar, B., Raina, A., Kaur, S., Dash, R. J., Samuel, E. and Datta, B. N. Clinicopathological study of testicular involvement in leprosy. Lepr. India **54** (1982) 48–55.

Twenty-five patients of lepromatous leprosy were studied clinically and histopathologically for testicular involvement. Testicular pain or swelling was the commonest complaint (68%) followed by sterility (28%) and impotence (4%). Reduced testicular size associated with soft feel was observed in 76% patients. Gynecomastia was present in 36% and altered sexual hair pattern in 24%. Eleven out of 16 (69%) patients had oligo/azoospermia. Out of the 20 testicular biopsies, 15 (75%) had definite histological evidence of leprous pathology, irrespective of testicular size, semen picture, and clinical signs and symptoms. One out of three epididymal biopsies showed minimal changes. Histopathological changes varied markedly, it was not possible to categorize these into vascular, interstitial and obliterative phases.—Authors' Summary

Kumar, B., Sehgal, S., Ganguly, N. K., Kaur, S. and Chakravarti, R. N. Total and differential serum proteins and globulins in leprosy. Lepr. India **54** (1982) 263–269.

Total and differential serum proteins were estimated in 177 adult male patients and globulins in 135 patients. Total serum proteins were slightly lowered in BB, BL, and LL patients. Total albumin was low in all types of leprosy, especially in the BL group. Alpha-1 and alpha-2 fractions were unchanged all through the leprosy spectrum. Beta globulins were significantly lowered in LL patients as compared to the controls. Gamma globulins were elevated in all types of leprosy, more so in BB, BL, and LL patients. Details are presented.—Authors' Summary

Malaviya, G. N., Mukherjee, A. and Ramu, G. Nerve abscess in lepromatous leprosy. Lepr. India **54** (1982) 123–129.

Six cases of nerve abscesses developing in patients of lepromatous leprosy are reported. The cases reported in literature have been reviewed and the pathogenesis of abscess formation is discussed.—Authors' Summary

Pacin, A., Fliess, E. L. and Llorente, B. La función hepática a través del espectro clinico de la hanseniasis. (Hepatic functions in relation to the clinical spectrum of hanseniasis.) Hansen. Int. **5** (1980) 93–111. (in Portuguese)

Liver function was studied in 100 hanseniasis patients. They were classified in the following ten groups: quiescent LL (20 patients), quiescent BL (13 patients), quiescent BB (7 patients), quiescent BT (9 patients), quiescent TT (12 patients), reactional

LL (12 patients), reactional BL (10 patients), reactional BB (7 patients), reactional BT (5 patients), and reactional TT (5 patients). A comparison was made with a control group (ten healthy individuals). A hyperproteinemia with high levels of globulin and normal levels of albumin in the serum was found in all clinical forms, and a typical pattern of "light damage hepatic cells" with elevations in the enzymatic activities of GOT, GPT, and alkaline phosphatase with no changes in turbidity tests and bilirubinemia, in all reactional patients. The physiopathology of this problem and the types III and IV hypersensitivity phenomena are discussed.—*Adapted from* the Authors' Summary)

Peyri, L. Baumann, E., Torras, A., Gonzalez, J. and Peyri, J. Fenómeno de Lucio en un caso de lepra lepromatosa paucinodular. (The Lucio phenomenon in a case of lepromatous paucinodular leprosy.) Actas Dermo-Sifiliogr. **73** (1982) 67.

Hemos tenido la ocasión de observar la aparición de una leprorreacción semejante al fenómeno de Lucio en un enfermo de lepra lepromatosa nodular con unas peculiares características.

Se trata de un varón de cuarenta y cuatro años, con antecedentes enólicos importantes, que ingresa en nuestro hospital por un cuadro de una semana de evolución, de malestar general, astenia, sensación febril con escalofríos y dolor en flanco izquierdo difícil de catalogar. En la exploración física de ingreso destaca un estado consciente, pero algo desorientado, una temperatura axilar de 39°C y una hepatoesplenomegalia de tres-cuatro traveses de dedo, con unos parámetros analíticos compatibles con su hepatopatía crónica.

A las cuarenta y ocho horas de su ingreso aparecen unas lesiones cutáneas distribuidas en ambas extremidades superiores e inferiores, consistentes en placas purpúricas y ampollas hemorrágicas, de base eritematosa e infiltrada, con bordes bien definidos, adoptando formas caprichosas, estelares o reticulares, que evolucionan formando costras y pequeñas ulceraciones.

Tras esta erupción, nos llamó la atención la presencia de unas lesiones maculopapulosas, eritematoparduzcas, en la cara anterior del tórax; un nódulo en el brazo derecho y otro en la región centrotorácica; la infiltración eritematosa de la frente y la hipertrofia de los lóbulos de las orejas, lo que nos hizo pensar en la posibilidad de la enfermedad de Hansen.

El enfermo ha residido toda su vida en Viladecáns (Barcelona) y la mujer procede de Baza (Granada), viviendo desde hace veinticinco años en Viladecáns. Desconocen si hay familiares enfermos.

En el frotis de la piel del tórax, frente, mucosa nasal y lóbulo de la oreja se observan abundantes bacilos ácido alcohol resistentes en todas las localizaciones. Biopsia de una lesión purpúrica: vasculitis leucocitoclásica a nivel de dermis e hipodermis; Ziehl-Neelsen: no se observan bacilos. Biopsia de un nódulo: leproma bien delimitado; Ziehl-Neelsen: gran cantidad de bacilos aislados y formando globis. Biopsia de una maculopápula centrotorácica: infiltrado histiocitario en bandas en la dermis; Ziehl-Neelsen: bacilos la mayoría en vías de destrucción. Biopsia de piel aparentemente sana: manguitos perivasculares de histiocitos; Ziehl-Neelsen: abundantes bacilos.

Estudio immunológico.—Gran aumento de IgG; disminución del complemento en la leprorreacción, normalizándose a la semana de tratamiento; la determinación de immunocomplejos por la técnica de Clq Binding Assay en fase liquida dio unos valores diez veces superiores a los sueros normales; la immunidad celular estaba deprimida; no se pudo realizar un test con lepromina.

Se inició tratamiento con talidomida, 100 mg cada ocho horas, desapareciendo a los nueve días de iniciado el tratamiento la fiebre de hasta 40° que se había mantenido hasta entonces, con resolución progresiva de sus lesiones cutáneas.

Creemos que el enfermo se podría clasificar dentro del espectro clinico, patológico e inmunológico que presenta la lepra, entre la lepra lepromatosa difusa, con una respuesta nula a nivel de la inmunidad celular, y el enfermo con un cierto grado de eficacia de la inmunidad celular que se traduciría por la presencia de múltiples lepromas bien delimitados. La leprorreacción que presenta el enfermo podría representar ya un fenómeno de Lucio de menor intensidad que el que se presenta en la lepra difusa, ya una

leproreacción de tipo 2 con unas características distintivas que remedan al fenómeno de Lucio.—(*From the* article)

Peyri, L., Baumann, E., Torras, A. and Peyri, J. El espectro de las leprorreacciones necrotizantes. (Vasculitis alérgica cutánea—Fénomeno de Lucio.) A propósito de una leprorreacción intermedia. [The spectrum of the necrotizing lepra reactions. (Allergic cutaneous vasculitis, Lucio phenomenon.) A proposed intermediate lepra reaction.] Rev. Leprol. **13** (1982) 383–390. (in Spanish)

A case of necrotizing lepra reaction considered a borderline type between a Lucio phenomenon and a cutaneous allergic vasculitis lepra reaction is presented by the authors. The different necrotizing lepra reactions and their relationships are reviewed.—Authors' Summary

Prabhu, S. R. and Daftary, D. K. Clinical evaluation of oro-facial lesions of leprosy. Trop. Dent. J. **4** (1981) 83–95.

Seven hundred leprosy patients were subjected to oral and facial examination for the occurrence of lesions of leprosy. It was found that 28.71% of the patients showed facial lesions; while 11.57% had clinically detectable oral lesions of the disease. The oro-facial lesions were correlated to the type, the duration of the disease, and the treatment. The intraoral lesions of the disease were in the form of ulcerations, nodules, atrophic areas and indurations of the mucosa while the facial lesions involved the nose, eyes, ears and the facial skin. It was found that the lesions tended to be more prevalent during the first five years of the disease.—Authors' Summary

Ramanujam, K. Tuberculoid leprosy or sarcoidosis? A diagnostic dilemma. Lepr. India **54** (1982) 318–323.

During an intensive survey in a leprosy endemic area in south India, a young male adult was detected with infiltrated skin lesions and diagnosed as a case of major tuberculoid leprosy. The presence of leprosy in the individual could not be clinically established, despite a histological diagnosis of tuberculoid leprosy made on his skin biopsy. In an 18-year follow up during which he was examined on six occasions, the skin patches continued very much the same in appearance with a progressive increase in size; he was re-biopsied from the same lesion three times and was declared tuberculoid or borderline tuberculoid leprosy. At no time did the clinical findings warrant a diagnosis of leprosy but suggested that it could be sarcoidosis or lupus vulgaris. The biopsy done for the fifth time from the same skin lesion during the seventh examination and from the site of Kveim test confirmed the condition to be sarcoidosis.—Author's Summary

Rao, C. K., Ramaprasad, K., Narasimham, M. V. V. L., Nath, V. V. N., Rao, C. K. and Sharma, S. P. General morbidity, leprosy, scabies and common cold in association with bancroftian filariasis in East Godavari district (A.P.). Indian J. Med. Res. **75** (1982) 667–672.

The population in four bancrofti endemic villages was studied for four years to understand the epidemiology of filariasis. The rate of general morbidity during the period was significantly higher among those with chronic filariasis than in microfilaria carriers and normals for each of the three age groups. Analysis of sickness during January–June, 1976, or by person-half-years during the whole period, revealed the same trend. The microfilaria carriers, chronic filariasis cases, and normals 50 years and older had the highest sickness rate; while those 15–49 years had the lowest.—(*Adapted from* the Authors' Summary)

Reddy, P. K. and Prabhudass, N. Nerve damage in tuberculoid leprosy. Lepr. India **54** (1982) 283–286.

The pattern of ulnar nerve damage was studied in 45 patients suffering from borderline tuberculoid leprosy. All the patients were subjected to sensory and voluntary muscle testings of the hands. It was observed that while all patients showed evidence of sensory and autonomic deficit in the ulnar nerve-supplied areas of the hands, only 40 patients showed evidence of motor deficit in the muscles supplied by the same nerve.

The probable mechanism of selective

sparing of motor function in the remaining five patients is discussed.—Authors' Summary

Sahasranam, K. V., Anand, I. S., Kumar, B., Kaur, S. and Wahi, P. L. Cardiovascular autonomic functions in leprosy. Indian J. Med. Res. **75** (1982) 332–336.

Cardiovascular autonomic functions were studied in ten patients with bacilli positive lepromatous leprosy and eight healthy adult controls. Recording of intra-arterial blood pressure was done by brachial artery cannulation. The effect of mental arithmetic, sudden loud noise, posture, cold pressor test and apneic face immersion in cold water, on the blood pressure and heart rate were noted. Valsalva maneuver was performed and the Valsalva ratio calculated. The baroreceptor sensitivity and the intrinsic heart rates were also determined. The results of these investigations showed no significant differences in the two groups. It is concluded that cardiac autonomic functions are not significantly affected in lepromatous leprosy.—Authors' Summary

Sahni, U., Reddy, B. S. N. and Malik, R. Clinico-pathological study of so-called immune zones in leprosy. Lepr. India **54** (1982) 256–262.

The clinical, bacteriological and histopathological features were studied in 20 cases of leprosy (10 LL + 10 BL) from the so-called immune zones, i.e., axilla, groin, and a narrow transverse band of skin over the lumbosacral region of the body. Apparently uninvolved skin over the chest was studied as a control site. In the so-called immune sites, the clinical lesions of leprosy were noted in 40% of the cases (7 LL + 1 BL); AFB (both solid and granular forms) were detected in the smears of 45% of the cases (8 LL + 1 BL), and histopathological evidence of the disease was observed in almost all the sites studied (100%). The results obtained in the present study revealed that practically no area on the surface of skin is immune to leprosy.—Authors' Summary

Seggie, J. and Gelfand, M. Renal amyloidosis complication of tuberculoid leprosy and plasma cell dyscrasia; case reports of three patients. Cent. Afr. J. Med. **28** (1982) 105–111.

Three African patients with the nephrotic syndrome due to renal amyloidosis are discussed. Together they exemplify the two major categories of amyloidosis: the first patient developed reactive systemic amyloidosis as a complication of chronic tissue necrosis associated with trophic ulceration in tuberculoid leprosy; the second and third patients represent cases of amyloidosis associated with immunocyte dyscrasia.—Authors' Summary

Taylor, P. M. The clinical diagnosis of dapsone resistant leprosy. Lepr. India **54** (1982) 117–122.

For the early recognition of dapsone resistance, it is essential to regularly examine patients at risk for suspicious new lesions, backed by regular clinical treatment records including smear results. The earlier the recognition and starting on alternative treatment, the better is the response. However, it is not advisable to change treatment without attempting at least clinical confirmation, and endorsing the chart so that the problem is not missed on subsequent occasions.—Author's Summary

Terencio de las Aguas, J. and Rubio, F. C. Transformacion de lepra lepromatose en dimorfa. (Transformation of lepromatous leprosy into dimorphous.) Rev. Leprol. **13** (1982) 401–413. (in Spanish)

Three cases of lepromatous leprosy, without any doubt of classification, are presented. After more than 15 years of the disease and after various years of bacteriologic negativity, these three cases relapsed due to incorrect therapy or because of their abandoning therapy. Upon relapse, these cases had clinical and histological features of the borderline form of leprosy. Other personal cases and cases which have been described in the literature which have undergone the same transformation are reviewed. These are explained as relapses into a more benign form of leprosy.—(*Translated from* Authors' Summary)

Immuno-Pathology

Bechelli, L. M., Haddad, N., Guimarães Pagnano, P. M. and Carminatti Fregnan, R. Corrélation entre les réactions précoces (Fernandez) et tardives (Mitsuda) chez des enfants et adolescents non-contacts et sans manifestations de lèpre, testés avec lepromine humaine et différentes concentrations de l'antigène du tatou en trois essais à double insu. [Correlation between early (Fernandez) and late (Mitsuda) reactions in children and adolescent non-contacts and without manifestations of leprosy, tested with human lepromin and different concentrations of armadillo antigen in three double-blind trials.] Acta Leprol. **86–87** (1982) 97–109. (in French)

The authors carried out three double-blind trials to determine the correlation between the early and the late lepromin reactions and to verify the practical and control values of the 48 hours or Fernandez reaction. Children and adolescent non-contacts were tested with human lepromin (40×10^6 bacilli/ml) and different concentrations of armadillo lepromin (160, 40, 20, 10, 5, 2.5 and 1×10^6 bacilli/ml). The conclusions are as follows:

a) The coefficients of correlation (r values) point out that the correlation between the two reactions is poor or almost null.

b) The negative or doubtful reactions, the most often observed, have no practical value because they are almost always followed by a positive Mitsuda reaction.

c) The positive Fernandez reaction was always followed by a positive Mitsuda reaction. Thus it has practical importance. However as the frequency of early positivity is low with human and armadillo lepromin of lower concentrations, recommended in routine testing, the 48 hours reading is unnecessary and without control value. It would represent a loss of time and money.—Authors' Summary

Closs, O., Reitan, L. J., Negassi, K., Harboe, M. and Belehu, A. *In vitro* stimulation of lymphocytes in leprosy patients, healthy contacts of leprosy patients, and subjects not exposed to leprosy. Scand. J. Immunol. **16** (1982) 103–115.

In vitro lymphocyte stimulation was performed on peripheral blood lymphocytes from 48 leprosy patients, 15 healthy contacts of leprosy patients, and 16 normal controls who lived in a leprosy-free area and who had not been exposed to leprosy. Tuberculin PPD and an antigen fraction, MLW 1, prepared from *M. leprae*, were used as stimulants. The MLW 1 preparation contained one antibody-precipitable component when tested in crossed immunoelectrophoresis against a polyvalent anti-*M. leprae* immunoglobulin preparation, namely the ML 7 antigen. MLW 1 induced strong lymphocyte responses in patients with tuberculoid leprosy and healthy contacts of leprosy patients, but only weak or no responses in lepromatous leprosy patients and non-exposed controls. A marked depression of the response to tuberculin PPD was observed in lepromatous leprosy patients. The specificity of the MLW 1 antigen is discussed, and a new estimator of specific lymphocyte stimulation, the Δcpm', is introduced.—Authors' Summary

Fotedar, A., Mustafa, A. S., Narang, B. S. and Talwar, G. P. Improved leucocyte migration inhibition response of leucocytes from lepromatous leprosy patients with hapten modified *M. leprae*. Clin. Exp. Immunol. **49** (1982) 317–324.

Two acetoacetylated derivatives of *Mycobacterium leprae* with variable hapten groups and a conjugate with tetanus toxoid were prepared. These were tested as antigens along with unmodified *M. leprae* in the leukocyte migration inhibition (LMI) response of leukocytes from clinically, bacteriologically, and histopathologically confirmed cases of lepromatous leprosy. LMI response was poor with *M. leprae*, but was significantly enhanced with acetoacetylated *M. leprae*.—Authors' Summary

Gillis, T. P. and Buchanan, T. M. Production and partial characterization of mono-

clonal antibodies to *Mycobacterium leprae*. Infect. Immun. **37** (1982) 172–178.

Monoclonal antibodies to *Mycobacterium leprae* were produced by the fusion of BALB/c splenocytes and lymph node cells to BALB/c myeloma (NSI/1) cells. Eleven monoclonal antibodies were characterized as to their reactivity with *M. leprae* and 18 other mycobacterial species by enzyme-linked immunosorbent assay and immunofluorescence. Two monoclonal antibodies reacted only with *M. leprae*, and the other nine showed unique patterns of reactivity by enzyme-linked immunosorbent assay. One monoclonal antibody (IIH9) reacted with a 68,000-dalton protein present in extracts from *M. leprae*, *M. tuberculosis* H37Rv, *M. gastri*, and *M. smegmatis*. Potential uses for these antibodies in serological tests and immunochemical analyses are discussed.—Authors' Summary

Gu Zhijie, *et al.* Preliminary study on the immunologic functions of lymph nodes in leprosy. Chin. J. Dermatol. **13** (1980) 134. (in Chinese)

The immunological changes in the lymph nodes of various types of leprosy (total of 29 cases) were studied. It was found that in LL and BL type patients cellular immunity was decreased but humoral immunity was normal or increased.

Based on PHA-stimulated lymphocyte transformation, erythrocyte rosette formation, dinitrochlorobenzene patch tests, tuberculin, and streptokinase-streptodornase skin tests, it was found that the defect in nonspecific cellular immunity was not complete in the LL type of leprosy.

Changes of argentrophile (reticular) fibers varied with changes in immunity in various types of leprosy. When immunologic function (especially cellular immunity) was low, the number of fibers was less and the structure of the fibers was obscure, uneven, broken, or absent.

The lipid content was determined in 22 specimens. In TT lipids were very low. With the leprosy type approaching the LL end, the liposomes gradually became enlarged, sometimes like a big ball, and the number of liposomes increased. This suggested that the lipid content might reflect the immunological status in leprosy.—(*Translation by* Dr. Y. T. Chang)

Guimarães Pagnano, P. M., Bechelli, L. M. and de Lima Filho, E. C. Test de transformation des lymphocytes (TTL) par la phytohémagglutinine, la lépromine et *M. leprae* chez des malades de lèpre lépromino-négatifs et positifs: valeur pronostique comparée avec celle de la lépromine. [Lymphocyte transformation test (LTT) by phytohemagglutinin, lepromin and *M. leprae* in lepromatous leprosy patients—negatives and positives: Prognostic value compared with that of lepromin.] Acta Leprol. **86–87** (1982) 83–95. (in French)

In order to study the prognostic value of the lymphocyte transformation test (LTT) by phytohemagglutinin, lepromin and *M. leprae* compared with the lepromin reactivity, the authors have employed that test in leprosy patients classified according to Madrid classification and grouped according to Mitsuda reaction performed in all the patients with 0.1 ml of 40×10^6 bacilli/ml suspension and read after 30 days according to Madrid and WHO group criteria. The study was performed in two phases: in the first one, the lymphocytes were cultured in a medium with 20% of homologous serum (serum of unaffected donor). In this phase, 61 leprosy patients were studied: 24 L, 9 TT, 18 TR, 4 B and 6 I; 33 with negatives or doubtful Mitsuda reaction, and 28 reactors (1+, 2+ and 3+). In the second phase, the lymphocytes were cultured in a medium with 20% of autologous plasma (plasma of the patient) and 53 leprosy patients were studied (27 L, 14 TT, 9 TR and 3 I), 32 with negative or doubtful Mitsuda reaction and 21 reactors. The lymphocytes were separated from the plasma by Ficoll-hypaque and the lymphocyte transformation was evaluated by uptake of ^{3}H-thymidine.

The conclusions were as follows:

a) In a culture medium with homologous serum there was no correlation between lepromin reactivity and indices of stimulation by PHA and *M. leprae*; with lepromin the lymphocyte transformation was significantly higher in the group of lepromin reactor patients.

b) In a culture medium with autologous plasma, the indices of stimulation by lepromin and also by PHA and *M. leprae* were significantly higher in the group of patients with positive lepromin reaction.

c) The differences observed between the results in autologous plasma and homologous serum would be caused by an inhibitor factor present mainly in lepromatous plasma.

d) These results suggest that to determine the prognosis in leprosy patients by the LTT utilizing PHA, lepromin and *M. leprae*, the cultures in autologous plasma would be the most indicated since in this medium there is a more evident correlation between the indices of stimulation and lepromin reactivity.

e) The LTT compared with lepromin-reaction does not seem to be a good indicator of the immune responsiveness of leprosy patients because in several of them, nonreactor, the indices of stimulation were high while in some reactors the indices were low. The lepromin reaction, more economic and of easier execution than the LTT, continues to be the most convenient method to determine the prognosis of leprosy patients.—Authors' Summary

Hee Chul Eun, Won Suk Kim, Hong Sik Kim and Do-Il Kim. A study of peripheral blood T and B lymphocytes in leprosy. Kor. Lepr. Bull. **14** (1981) 13–20. (in Korean)

In leprosy, it is generally believed that the defense against *Mycobacterium leprae* is largely dependent on cell-mediated immunity (CMI) and there is an accumulating evidence that patients with lepromatous leprosy have not only defective CMI specific for *M. leprae* but also have generalized impairment of CMI. In contrast the humoral immune reactivity, both specific and nonspecific, has been found to be normal or slightly increased.

Recently, several investigators have enumerated the peripheral blood T and B lymphocytes in patients with leprosy; however, there is no agreement as to the results. Furthermore, leprosy has been found to differ in its clinical manifestations and immunological behaviors in different geographic areas and races. Nevertheless, there is yet no report in Korea concerning T and B lymphocyte enumeration.

Eighty-nine patients with leprosy (37 polar lepromatous, 17 borderline lepromatous, 17 borderline tuberculoid, and 18 polar tuberculoid) were entered in this study. The diagnosis of leprosy was made by clinical, bacteriological, histopathological, and immunological assessment and the patients were classified according to the Ridley-Jopling scale. All patients were under antileprosy chemotherapy with diamino diphenyl sulfone (DDS) for varying periods, 6 months to 26 years. The normal healthy control group included 33 medical students, physicians, and nurses. Peripheral blood T and B lymphocytes were enumerated by the E-rosette technique and mouse red blood cell (MRBC)-rosette technique, respectively. The results were summarized as follows:

a) The mean percentage of total T lymphocytes was 66.2% in patients with LL, 69.1% in BL, 70.4% in BT, and 71.9% in TT, respectively. The mean percentage of T lymphocytes in the normal control group was 72.0%. There was a statistically significant decrease in the percentage of T lymphocytes in LL patients, as compared with normal healthy controls ($0.01 < p < 0.025$).

b) The mean percentage of B lymphocytes was 8.0% in patients with LL, 6.5% in BL, 6.6% in patients with BT and TT, and 5.7% in normal healthy control group. There was a statistically significant increase in the percentage of B lymphocytes in patients with LL ($p < 0.05$).

c) There was no statistically significant difference in the percentage and absolute counts of T and B lymphocytes between patients with erythema nodosum leprosum (ENL) and patients without it.

d) There was no statistically significant difference in the percentage of T and B lymphocytes between lepromatous patients receiving antileprosy chemotherapy for less than three years and more than three years.—Authors' Summary

Hua Wenyuan, *et al.* Study of microcirculation of the nail folds of leprosy. Chinese J. of Dermatol. **4** (1982) 14. (in Chinese)

By means of a capillaroscope of the authors' design, the microcirculation in the nail

folds of 56 leprosy patients was studied. In about 80% of the cases there were morphological abnormalities in capillary loops and relatively obvious changes in patterns of blood flow. These changes were mainly found in patients with lepromatous disease with lesser frequencies in borderline and tuberculoid cases. Among the lepromatous patients, these changes were more severe in late cases than in those cases in an early stage of the disease. These abnormalities in the microcirculation of the nail folds seem to mainly depend on the type and stage of leprosy rather than on the presence or absence of claw deformities.—(*Adapted from* the Authors' Summary)

Kano, K., Aranzazu, N., Nishimake, T., Convit, J., Albini, B. and Milgrom, F. Serological and immunohistological studies on lepromatous leprosy. Int. Arch. Allergy Appl. Immunol. **64** (1981) 19–24.

Sera of patients with lepromatous leprosy were studied for the presence of a variety of antibodies and immune complexes (IC). The frequencies of heterophile, Hanganutziu-Deicher and Forssman antibodies were 61% and 43%, respectively, which were significantly higher than those in other diseases. The frequency of antibodies to cardiolipin was 89% and the frequency of rheumatoid factor was 34%. Circulating IC were demonstrated in 54% of the patients' sera by Raji-cell test and in 43% by anti-antibody inhibition test. Analyses of immunoglobulin classes of IC revealed that IgG was predominant in IC of patients with lepra reaction (LR) and IgM in patients without LR. Immune deposits were found in and between cells of dermis in skin biopsy specimens of patients with LR.—(*From* Trop. Dis. Bull.)

Karazawa, E. H., Proença, N. G., Mimica, I., Kliemann, T. A. E., Martinez, E. W., Guedes, M. and Rarias, L. R. Estudo comparativo da intradermo-reaçāo praticada com lepromina integral e com lepromina tratada por ultrasom em individuos normais. (A study comparing the intradermal reactions following integral lepromin and lepromin treated with ultrasound in normal individuals.) Hans. Int. **5** (1980) 123–128. (in Portuguese)

A comparative study on the Fernandez and on the Mitsuda reaction was made in 104 normal people employing whole and sonicated lepromin. Both types of lepromin can induce a good early reaction, and there was no significant difference in the results of the Fernandez reaction. The sonicated lepromin, although it contains all of the components of the original preparation, gives weaker late skin reactions. The results of the Mitsuda reaction were statistically significant.—Authors' Summary

Liu Zijun, *et al.* Histopathology of primary indeterminate leprosy. Chin. J. Dermatol. **13** (1980) 129. (in Chinese)

Histopathological studies were made on the skin lesions of 51 primary indeterminate leprosy patients observed over a number of years in our institutions. All specimens were re-sectioned and stained. Bacillary distribution and cellular changes in the epidermis, dermis, and various epidermal appendages (sweat glands, sebaceous glands, and arrector pili) were described. Quantitative determination on the cellular infiltration was made, and the ratio of the area of cellular infiltration against the area of dermis was given. A ratio of higher than 1/21 was observed in 70% of all lesions. This value was higher than the upper limit of 1/20 given by Ridley for the early lesions in leprosy. Leprosy bacilli were observed in 20 cases. Pathological changes in the small nerves were observed in 49 cases. Diagnosis of primary indeterminate leprosy should be based on the presence of leprosy bacilli and/or pathological changes in the small nerves. Bacillus-positive lesions exhibited a high level of immunity and bacillus-negative lesions, a low level of immunity. More mast cells were observed in the primary indeterminate lesions than in any other types of leprosy. While the appearance of leprosy bacilli in the epithelial cells favors the view that the organisms make their entry via the epithelium, the occurrence of multiple foci in the dermis might also indicate that the infection is distributed through blood circulation.—(*Translation by* Dr. Y. T. Chang)

Liu Zijun, *et al.* Ultrastructures of cells in lesions of lepromatous and tuberculoid leprosy. Chin. J. Dermatol. **13** (1980) 209. (in Chinese)

Electron microscopic (EM) stuides were performed on the skin lesions of ten LL and four TT leprosy patients. Ultrastructures of lepra cells, epithelioid cells, and Langerhans'-type giant cells were described. Lepra cells contained only a few organelles in the cytoplasm, such as mitochondria, lysosomes, endoplasmic reticulum, and Golgi apparatus. Epithelioid cells revealed more abundant cytoplasmic organelles. Langerhans'-type giant cells showed a morphology similar to that observed in tuberculosis. These cells revealed more abundant cytoplasmic organelles than epithelioid cells. While various numbers of leprosy bacilli were observed in lepra cells, there were none in the epithelioid and Langerhans'-type giant cells. This suggested that both epithelioid and Langerhans'-type giant cells probably played an important role in the destruction and digestion of leprosy bacilli in leprosy. The authors were not aware of any report on EM studies of Langerhans'-type giant cells in leprosy.—(*Translation by* Dr. Y. T. Chang)

Nanda, N. K. and Nath, I. Specific modulation of antigen stimulated human lymphocyte response by histamine. Indian J. Med. Res. **75** (1982) 703–711.

Peripheral blood lymphocytes derived from 22 normal, tuberculin sensitive human volunteers were stimulated *in vitro* with optimal and suboptimal concentrations of the specific antigen (PPD). Addition of histamine over a range of concentrations from 10^{-9} to 10^{-1} M had varying effects on *in vitro* lymphocyte proliferation. The enhancement of antigen-induced DNA synthesis at two concentration ranges of histamine was a significant finding. Individuals studied showed maximal increment of *in vitro* PPD responses at the lower range of 10^{-8} to 10^{-6} M and at the higher range of 0.7×10^{-3} to 6×10^{-3} M. This increment was specific since cimetidine—an antagonist to histamine-2 type receptor—abrogated the effects of histamine.—Authors' Summary

Pilot-trial of treatment of leprosy by pig's thymosin combined with dapsone. Acta Acad. Med. Sinicae **3** (1981) 198–200. (in Chinese)

Six leprosy patients (1 LL, 4 BL, and 1 BB) were treated with thymosin (ThFs) and standard dapsone (DDS) therapy. All of these patients showed clinical and pathological improvements. Results showed that immunotherapy associated with chemotherapy was better than DDS therapy alone. One DDS-resistant case of BL leprosy with histoid leproma also obtained a satisfactory result. Reversal reactions occurred in two patients. Erythema nodosum leprosum was noted in three. No other side-effect was noted.—(*Adapted from* Summary)

Ridley, M. J. and Russell, D. An immunoperoxidase study of immunological factors in high immune and low resistance granulomas in leprosy. J. Pathol. **137** (1982) 149–157.

The epithelioid cell granuloma in high resistant tuberculoid (TT) leprosy was contrasted with the pure macrophage granuloma of anergic lepromatous leprosy (LL) by evaluating various immunological factors operating in these lesions. The immunoperoxidase technique using antisera to immunoglobulin IgG, IgM, complement C3, C3d and C1q and other products of macrophage secretion, lysozyme, plasminogen, a_1 antitrypsin and C-reactive protein and of Ia antigens revealed peak levels in tissues of most of these factors in both types of granuloma. The tuberculoid response was linked to low antigenic load and Ia-like antigen and the lepromatous response was secondary to a high antigenic load in the absence of Ia antigen.

Complement and other mediators were found intracellularly in both tuberculoid and lepromatous granulomas, but extracellularly only in tuberculoid lesions. This may indicate local hypersensitivity in the tuberculoid granuloma. It is suggested that the mediators in LL macrophages remain bound to the lipids of mycobacterial degeneration in the phagocytic vacuole.

Secretory cells were differently sited in the two types of granulomas: peripheral in epithelioid cell lesions and central around

capillaries over the whole lesion in pure macrophage granulomas of LL. In tuberculoid leprosy many of the central vessels in the granuloma were obliterated.

C1q was found in fibroblasts. However, the marked absence of fibrosis in any of the lesions of leprosy, except following severe reactions, casts some doubt on the link which has been postulated between epithelioid cells and fibroblasts as an explanation of fibrosis in granulomas.—Authors' Summary

Saha, K., Mittal, M. M. and Maheswari, H. B. Reversion of the downhill course of active lepromatous leprosy by repeated transfusions of fresh blood, donated by healthy but lepromin positive patients. Transfusion (Philadelphia) **22** (1982) 134–137.

Earlier studies of immunologic reconstitution therapy of active lepromatous leprosy patients by repeated infusions of viable allogeneic blood lymphocytes indicated a beneficial effect. In order to avoid cell separation and its associated risks, we attempted to transfer immunity passively into seven seriously ill lepromatous patients by repeated transfusions of fresh blood donated by healthy, but tuberculin and lepromin positive, subjects. The results showed clinical improvement in some cases with the elimination of *Mycobacterium leprae*, histological reversion, and return of immunologic responsiveness.—Authors' Summary

Sakuntala, R., Pratap, V. K., Sharma, N. K., Dayal, S. S. and Aggarwal, S. K. Histologic profile in apparently normal skin of leprosy patients. Lepr. India **54** (1982) 40–47.

In apparently uninvolved skin of 42 leprosy patients infiltration around the skin appendages, blood vessels, nerves and in subepidermal region along with erosion of basal layer, and desquamation of superficial epidermis and vacuolization was observed. Delineation of nerve fibers and Schwann cell hyperplasia were recorded in 21 and 16 cases, respectively. Subepidermal granuloma harboring lepra bacilli was a significant finding in three cases.—Authors' Summary

Sengupta, U., Sinha, S., Ramu, G., Mukherjee, A. and Desikan, K. V. Assessment of Dharmendra antigen. (V) Attempts for purification of specific skin delayed hypersensitivity (DH) inducing antigen(s) from lepromin. Lepr. India **54** (1982) 208–213.

After electrophoresis (in pyrogen-free conditions) of Dharmendra antigen sonicates on agarose gel slides, the components (anionic and cationic) were eluted in pyrogen-free normal saline. On skin testing, it was found that only the anionic component produced specific skin reactions in tuberculoid leprosy patients. The significance of the observations is discussed.—Authors' Summary

Shannon, E. J., Powell, M. D., Jacobson, R. R. and Hastings, R. C. Investigacion de los mechanismos supresores en la lepra. (An investigation of suppressor mechanisms in leprosy.) Dermatologia (Mexico) **25** (1981) 457–468. (in Spanish)

Polar lepromatous leprosy (LL) is characterized by the absolute non-detectability of cell-mediated immunity (CMI) to *M. leprae*. The nature of this antigen specific T cell deficiency is unknown. One hypothesis is that the defect is genetically determined and therefore cannot be corrected with a vaccine consisting of *M. leprae* itself. Another hypothesis is that LL individuals are capable of recognizing *M. leprae* antigens but effective CMI is prevented by suppressor cells, in which case a vaccine based on *M. leprae* may be effective. We have studied the ability of Dharmendra antigen(s) to result in suppression of lymphocyte proliferation in response to concanavalin-A (Con-A) *in vitro*. By various methods of analysis, using various doses of Con-A, apparent suppression can be seen in lepromin skin test positive healthy subjects, inactive leprosy patients, active tuberculoid leprosy patients, and (in one instance) LL patients with erythema nodosum leprosum (ENL); but not in healthy naive subjects, or in leprosy patients with borderline or uncomplicated lepromatous disease. Considerable reservations are in order regarding whether or not this experimental system accurately reflects

clinically relevant *in vivo* phenomena. If suppressor cells are present in borderline and tuberculoid leprosy patients, they could act to prevent Type I or reversal reactions, and if present in LL, to prevent Type II or ENL reactions. In our view firm conclusions regarding the possible role of the suppressor cells in the pathogenesis of LL cannot be made at this time. In the absence of agreement on the pathogenesis of the infectious, multibacillary form of leprosy, optimal strategies for a leprosy vaccine can be expected to remain controversial.—Authors' Summary

Sinha, S., Sengupta, U., Ramu, G. and Desikan, K. V. Assessment of Dharmendra antigen. (VI) Skin tests with fractionated nucleic acids. Lepr. India **54** (1982) 214–219.

Leprosy patients were skin tested for induction of skin delayed type hypersensitivity (DTH) with various preparations of Dharmendra antigen (DA) (sonicated antigen, DNA + RNA and DNA). Extracted nucleic acids produced smaller reactions (including some negative ones) as compared to sonicated whole antigen (which included proteins). BCG fractions, prepared similarly, produced non-specific skin reactions.—Authors' Summary

Srinivasan, H., Rao, K. S. and Iyer, C. G. S. Discrepancy in the histopathological features of leprosy lesions in the skin and peripheral nerve. Report of a preliminary study. Lepr. India **54** (1982) 275–282.

Simultaneous biopsies of the skin and a cutaneous nerve were done in 36 randomly selected leprosy patients, and the histopathological features of the lesion in the two tissues were compared. A discrepancy was noticed in 21 instances. In 19 of these cases the lesions in the nerve were found to be immunologically more deficient and were also bacillated, even when the skin lesion had cleared or regressed. The implications of the findings are discussed and the need for further studies is emphasized.—Authors' Summary

Stoner, G. L., Mshana, R. N., Touw, J. and Belehu, A. Studies on the defect in cell-mediated immunity in lepromatous leprosy using HLA-D-identical siblings. Absence of circulating supressor cells and evidence that the defect is in the T lymphocyte, rather than the monocyte, population. Scan. J. Immunol. **15** (1982) 33–48.

Sixteen healthy siblings were identified as HLA-D-identical to 12 borderline lepromatous or polar lepromatous patients by the absence of a mixed lymphocyte reaction (MLR). The peripheral blood mononuclear cells (PBM) of the healthy siblings showed a lymphoproliferative response (Δcpm) to *Mycobacterium leprae* antigens which was about fivefold or more greater than that of the lepromatous patients. Lepromatous PBM, with or without mitomycin C treatment, were co-cultured with a constant number of normal PBM. In other experiments the two cell types were co-cultured in various proportions, with the total cell number kept constant. Neither approach revealed suppressor cells in lepromatous PBM capable of suppressing the lymphoproliferative response to *M. leprae*. On the contrary, we found that lepromatous PBM can respond to *M. leprae* antigens if the sensitized lymphocyte is provided by mitomycin-C-treated normal PBM. Additionally, experiments in which isolated adherent cells and non-adherent cells of sibling pairs were recombined failed to reveal a defect in the *M. leprae* antigen-presenting function of lepromatous adherent cells. Since we found no evidence that sensitized cells are present in lepromatous PBM with their function unexpressed (due to a monocyte defect) or suppressed (due to suppressor cells), we conclude that lepromatous patients simply lack sufficient numbers of antigen-specific T lymphocytes to initiate a lymphoproliferative response to *M. leprae* antigens. The reason for their absence remains an important unanswered question.—Authors' Summary

Touw, J., Langendijk, E. M. J., Stoner, G. L. and Belehu, A. Humoral immunity in leprosy: Immunoglobulin G and M antibody responses to *Mycobacterium leprae* in relation to various disease patterns. Infect. Immun. **36** (1982) 885–892.

A solid-phase radioimmunoassay, applying whole *Mycobacterium leprae* as antigen and radiolabeled protein A from *Staphylococcus aureus* as antibody-detecting reagent, was used for the determination of specific immunoglobulin G (IgG) and IgM antibody responses in leprosy patients. High IgG anti-*M. leprae* antibody levels were found in lepromatous leprosy patients; whereas the antibody response in tuberculoid leprosy patients varied from negative, i.e., comparable with responses measured in normal individuals, to strongly positive. In tuberculoid leprosy patients, a significant increase in IgG anti-*M. leprae* antibody levels was observed in the more widespread forms of the disease, but positive antibody responses were especially predominant among patients with active lesions. Lepromatous leprosy patients generally demonstrated high levels of both IgG and IgM anti-*M. leprae* antibodies, but no relation was found between the antibody responses and bacillary load or other clinical parameters. A marked decrease in specific IgG and IgM antibody levels was observed in lepromatous leprosy patients during their first year of treatment. Differences in mechanisms regulating the humoral immune response in tuberculoid and lepromatous leprosy patients were indicated, and the application of antibody assessments in leprosy control programs is discussed.—Authors' Summary

Microbiology

Coudert, J., Lu, H. T. and Minjat, M. Souches myco-bactériennes adaptées à la culture à partir de lépromes humains. Caractères d'identification vis-à-vis de *Mycobactérium leprae*. (Mycobacterial strains adapted to cultures separated from human lepromas. Identifying characteristics vis-a-vis *Mycobacterium leprae*.) Acta Leprol. **86-87** (1982) 47–57.

Deux souches cultivables de mycobactéries isolées de cultures cellulaires de lépromes humains, sont comparées avec *M. leprae* et *M. lepraemurium* d'une part, avec *M. aquae* et *M. scrofulaceum* d'autre part. L'ultra-structure, le comportement intracellulaire, le rôle pathogène pour les rongeurs et surtout les caractéristiques immunologiques ont été étudiées. Les méthodes d'immunofluorescence et d'immuno-électrophorèse, vis-à-vis de sérums de malades ou d'animaux hyperimmunisés font ressortir une étroite parenté structurale et antigénique avec *M. leprae* et *M. lepraemurium*, et une absence d'identité avec *M. aquae* et *M. scrofulaceum*.—Authors' Summary

Delville, J., Spina, A., Rayyan, W., Cocito, C., Saint-André, P., Niamien N'Deli, L. and van Droogenbroeck, J. Propriétés morphologiques et biologiques des organismes diphthéroïdes (LDC) isolés chez les lépreux. [Morphologic and biologic properties of diphtheroid organisms (LDC) isolated in leprosy patients.] Acta Leprol. **86–87** (1982) 59–68. (in French)

Acid-alcohol-fast bacteria are not always detectable in all leprosy lesions. Non-acid-fast microorganisms may be associated with acid-fast bacteria. The most frequently isolated strains from leprosy lesions are non-acid-fast bacteria, morphologically related to *C. diphtheriae*. Hence their designation as diphtheroids or LDC (leprosy derived corynebacteria). Their antigenic structure is more closely related to *M. leprae* and other mycobacteria than to classical corynebacteria. This leads to the hypothesis of a potential role in the pathogenesis of leprosy and their use as an antigen for skin tests by leprosy patients.—Authors' Summary

Dutta, A. K., Katoch, V. M., Sharma, V. D. and Bharadwaj, V. P. Biochemical correlation of *M. vaccae* with *M. leprae*. Lepr. India **54** (1982) 234–241.

The biochemical tests, namely, niacin, catalase, nitrate reduction, Tween hydrolysis, tellurite reduction, arylsulfatase and urease tests, were carried out for all the mycobacteria which are immunogenically closely related to *M. leprae*. Among them only *M. vaccae* shows closest relationship with *M. leprae* when compared with its communicated data. Except for the tellurite reduction test which was variable in the case

of *M. leprae*, all other tests were found similar to that of *M. leprae*. In the next experiment, the thin-layer chromatographic pattern of mycolates from *M. vaccae* has been compared with that of *M. leprae*. The presence of keto-mycolate in the cell wall structure of both *M. vaccae* and *M. leprae* also reflects their biochemical relationship at the ultrastructural level.—Authors' Summary

Grosset, J., Guelpa-Lauras, C. C. and Lecoeur, H. Données actuelles sur la bactériologie de la lèpre. (Present data on the bacteriology of leprosy.) Acta Leprol. **86–87** (1982) 35–45. (in French)

Microscopic examination and mouse foot pad inoculation are the main tools in *Mycobacterium leprae* bacteriology. Microscopic examination enables us to calculate bacteriological and morphological indexes. The former scores the density of acid-fast organisms in the lesions and the latter scores their viability since only solidly stained acid-fast organisms are likely to be alive.

Mouse foot pad inoculation provides the opportunity for studying the growth curve of *M. leprae*. Alterations of this growth curve under drug therapy enable us to assess the antileprosy activity of drugs and to determine the drug sensitivity of organisms. Acquired and primary drug resistances to dapsone (DDS) are to date the most important events in the chemotherapy of leprosy.

Research is in progress on mice with congenitally reduced immunological capacity (nu/nu mice) and on antileprosy vaccination. Although no decisive advances have been obtained in these fields, the research in progress is promising.—Authors' Summary

Ishaque, M. Mycobacteria of *Mycobacterium scrofulaceum* type isolated from rat or mice lepromata are not the aetiologic agents of murine leprosy. Microbios **33** (1982) 35–44.

Mycobacterial strains M.M4 and M.EY3 were isolated from a mouse leproma, respectively, on KI-1 and Ogawa egg-yolk medium. Strain M.M4 was scotochromogenic and produced a yellow pigment. Young cultures were non-acid-fast and became acid-fast during the exponential growth phase. Primary cultures of strain M.M4 did not grow on conventional culture media. However, the subcultures grown in KI-1 medium were easily subcultured in the homologous media as well as on Löwenstein, Sauton and Dubos media. Cultures M.M4 were insensitive to isoniazid and *p*-nitrobenzoic acid. Both scotochromogenic strains M.R56 and M.M4 did not produce murine leprosy disease in susceptible animals like BALB-c and C3H mice.

Primary as well as the subcultures of strain M.EY3 grew only on the Ogawa egg-yolk medium. Colonies of this strain were creamy white and, unlike other mycobacteria, produced rust-like brown spots on the medium at the sites of colonies. *In vitro* grown cultures M.EY3 were sensitive to isoniazid and *p*-nitrobenzoic acid. BALB/c and C3H mice infected with M.EY3 cultures developed lepromata similar to those produced by the *in vivo* grown *M. lepraemurium*. Both M.R56 and M.M4 scotochromogenic cultures grown in liquid KI-1 medium are not the causative agents of murine leprosy. On the other hand, cultures M.EY3 grown on Ogawa egg-yolk medium possess characteristics similar to *M. lepraemurium* and are, in fact, the etiologic agents of murine leprosy.—Author's Summary

Kaur, S., Kumar, B., Ganguly, N. K. and Chakravarti, R. N. Viability of *M. leprae* under normal and adverse atmospheric conditions. Lepr. India **54** (1982) 228–233.

Harvested bacilli from fresh lepromas were subjected to drying at room temperature for varying periods, were exposed to direct sun-rays, UVR, and were then injected into the foot pads of thymectomized irradiated mice for checking the viability. The organisms could survive UVR for 30 minutes, direct sunlight for 2 hours and room temperature for 7 days. Details are presented.—Authors' Summary

Khanolkar, S. R., Ambrose, E. J. and Mahadevan, P. R. Uptake of 3,4-dihydroxy[^{3}H]phenylalanine by *Mycobacterium leprae* isolated from frozen (−80°C) armadillo tissue. J. Gen. Microbiol. **127** (1981) 385–389.

Mycobacterium leprae separated from armadillo tissues stored at −80°C is similar to that from human sources in its ability to take up ^{3}H-labelled 3,4-dihydroxyphenylalanine (DOPA). Several inhibitors were studied which showed complete or partial inhibition of [^{3}H]DOPA uptake. These findings suggest that *M. leprae* isolated from frozen tissue possesses an active uptake system for [^{3}H]DOPA.—Authors' Summary

Lancaster, R. D., Colston, M. J., Hilson, G. R. F. and Turner, S. M. The effect of body temperature and cell-mediated immunity on the growth of *Mycobacterium marinum* and *Mycobacterium leprae* in mice. J. Med. Microbiol. **14** (1981) 493–500.

Evidence is presented that the high susceptibility of armadillos to infection with *Mycobacterium leprae* cannot be explained solely in terms of body temperature because mutant mice maintained with a body temperature similar to that of armadillos do not become heavily infected with *M. leprae*. The depression of cell-mediated immunity accompanying the low body temperature is not sufficient to produce an overwhelming infection. The results obtained with *M. marinum* suggest that whereas lack of cell-mediated immunity or a low body temperature result in a moderately enhanced infection in the mouse, a combination of both of these factors is required to produce an overwhelming infection involving the internal organs.—Authors' Summary

Matsuo, Y. and Tatsukawa, H. Attempts at cultivation of *Mycobacterium leprae* in cell culture under regulation of redox potential at environment. Hiroshima J. of Med. Sci. **31** (1982) 141–143.

Cultivation of *Mycobacterium leprae* in cell culture was attempted under lower redox potential by adding such reducing agents as reduced glutathione, DL-cysteine hydrochloride, and dithiothreitol to culture medium, and by reduced oxygen tension varying the depth of medium or applying agar suspension technique. During a five-year period since 1976, a slight increase in the number of acid-fast bacilli at harvests was occasionally observed. However, the viability of bacilli recovered was unable to be proven by the mouse foot pad method. It is uncertain whether lower redox potential at environment is strictly requested for cultivation of *M. leprae*.—Authors' Summary

Nakamura, M. Effect of pantoyl lactone on the growth of *Mycobacterium lepraemurium* in cell-free liquid medium. Jpn. J. Lepr. **50** (1981) 139–140. (in Japanese)

Pantoyl lactone has been shown to have a cytokinetic effect on the long multinucleate filaments of certain mutant strains of *Escherichia coli* induced after exposure to radiation. The effect of pantoyl lactone on the growth of *Mycobacterium lepraemurium* in cell-free medium was tested in order to see whether pantoyl lactone had the same effect on *M. lepraemurium* as on filamentous *E. coli*. The results obtained were:

a) The numbers of bacilli in NDO-5 medium were significantly increased by addition of 0.005 M pantoyl lactone.

b) Remarkable growth stimulation of *M. lepraemurium* in the slide culture system was observed when 0.005 M pantoyl lactone was added.

c) However, filament formation of *M. lepraemurium* was still not changed by additions of any dose of pantoyl lactone.—(*Adapted from* Author's Summary)

Sanabria Negrin, J. G., Kouri Flores, J. B. and Smirnova, T. Estudios del *M. leprae* aislado de linfa de un paciente lepromatoso LL_p mediante la técnica de criofractura. (Studies of *M. leprae* isolated from the lymph of a lepromatous leprosy patient by means of the freeze-fracture technique.) Rev. Cub. Med. Trop. **33** (1981) 13–18. (in Spanish)

A study of *Mycobacterium leprae* isolated from the lymph of a lepromatous leprosy patient by means of the freeze-fracture technique was performed. Cell wall characteristics were visualized and compared with those from *M. bovis* (BCG) and *M. tuberculosis* H37Rv studied previously. The presence of mesosomes in the cytoplasm of these bacteria was corroborated and their origin from an invagination of the plasma membrane was proved.—(*Adapted from* Authors' Summary)

Saoji, A. M. and Kelkar, S. S. Anomalous isoenzymes of lactate dehydrogenase in sera of patients with leprosy. Lepr. India **54** (1982) 62–68.

In an earlier study (Saoji, *et al.* 1980) we looked for anomalous (additional) isoenzymes in homogenates of 17 active and 25 regressing lepromatous leprosy, 3 erythema nodosum leprosum, 8 BT, 19 TT and 1 indeterminate leprosy. Anomalous bands were found in 17 cases. They correlated with large numbers of viable organisms and were thought to originate from *Mycobacterium leprae*. This communication describes the serum LDH isoenzymes of the same 78 cases. Six of 17 cases with anomalous LDH isoenzymes in tissues showed anomalous bands even in serum samples. The bands were much fainter but had similar mobility in terms of Ef values. Therefore, LDH isoenzymes originating from *Mycobacterium leprae* were discernible in sera of cases, though not on the same scale as in the tissues.—Authors' Summary

Wheeler, P. R. and Gregory, D. Superoxide dismutase, peroxidatic activity and catalase in *Mycobacterium leprae* purified with armadillo liver. J. Gen. Microbiol. **121** (1980) 457–464.

Superoxide dismutase has been identified and peroxidatic activity demonstrated in *Mycobacterium leprae*. The superoxide dismutase, shown indirectly to be a manganese-containing enzyme, was present at low activity in the cell-free extract. Peroxidatic activity was detected in a hemoprotein on polyacrylamide gels, but quantitative assay was not possible. Catalase, although present in a cell-free extract, appeared to be a host-derived enzyme, thus emphasizing the importance of establishing the authenticity of enzyme activities in host-derived *M. leprae*. The implications for the growth of *M. leprae in vivo* and its non-cultivability are discussed in the light of these findings.—Authors' Summary

Experimental Infections

Bhat, R. and Vaidya, M. C. Nerve damage in leprosy—A teased fibre study of sciatic nerves in experimental mice. Lepr. India **54** (1982) 33–39.

The extent of nerve damage was assessed in the sciatic nerves of CBA/J mice with experimental leprosy by the teased single fiber preparations. Morphological changes in the fibers were observed up to 15 months of infection and compared with control animals of the same age groups. During a 4–9 month period, the fibers showed paranodal enlargements, widening of the Schmidt-Lantermann incisures, paranodal and whole segmental demyelination. In addition, fragmentation of axons with the formation of myelin ovoids in the Schwann tubes was also observed in animals with 9–15 months of infection. While segmental demyelination was predominant early in infection, axonal degeneration was more evident in advanced infection. These findings may possibly explain the underlying mechanism of nerve damage in human leprosy.—Authors' Summary

Colston, M. J. and Kohsaka, K. The nude mouse in studies of leprosy. In: *The Nude Mouse in Experimental and Clinical Research*. Vol. 2. Fogh, I. and Giovamella, B. C., eds. New York: Academic Press, 1982, pp. 247–266.

When inoculated in the foot pad with the human leprosy bacillus, *Mycobacterium leprae*, the nude mouse develops a greatly enhanced infection as compared to normal mice and, unlike in normal mice, there is widespread dissemination of the infection, with dense bacillary infiltration of the cooler body sites (such as tail, ears, etc.) and of the lymph nodes. Small numbers of organisms are detectable in the liver and spleen. Histopathologically, lesions in the nude mouse are similar to those in lepromatous leprosy patients. Preliminary experiments indicate that the response of infected nude mice to the antileprosy agents dapsone and rifampin is similar to that of lepromatous leprosy patients, and that the nude mouse is more sensitive than thymectomized-irradiated mice and normal mice for

detecting small numbers of viable organisms against a background of large numbers of dead organisms. These results suggest that the nude mouse should be of great value as a model for leprosy chemotherapy studies.—Authors' Summary

Hirooka, Y., Ohsawa and Saito, N. The strain difference of immune responses in mice infected with *Mycobacterium lepraemurium*. Jpn. J. Lepr. **50** (1981) 144–153.

One of the most susceptible strains, C3H mice, and the most resistant strain, C57BL/6 mice, were inoculated with 5×10^9 bacilli of *Mycobacterium lepraemurium* (Mlm) subcutaneously and lymphocyte transformation test of spleen cells to the specific antigen and polyclonal mitogens was performed, and DTH to PPD and unrelated antigen, SRBC and HGG, was also tested at various stages during the course of infection.

In LTT to the specific antigen, Mlm, C3H mice showed a very low response until 24 weeks after infection; although C57BL/6 mice showed high responses at 7, 8, and 13 weeks. In contrast, in LTT to T cell mitogens, PHA and Con-A, C3H mice developed the blastogenic response as high as seen in C57BL/6 mice, even at 24 weeks after infection, although C3H mice were heavily loaded with bacilli at this stage.

Response to B cell mitogen, LSP, was higher in C3H mice than in C57BL/6 mice.

Delayed-type hypersensitivity responses to Mlm and PPD measured in the foot pad were high in C57BL/6 mice at 7 weeks after Mlm infection. C3H mice also developed response to PPD in spite of low responsiveness to the specific antigen, Mlm.

DTH response to unrelated antigens, SRBC and HGG, were tested in Mlm-infected C3H mice. DTH to SRBC at 13 and 17 weeks was not different between Mlm-infected and uninfected control mice. DTH to HGG at 17 weeks was also the same as that of control mice.

These results showed that Mlm-infected C3H mice were not able to respond to the specific antigen, Mlm, but general depression of cell-mediated immunity was not observed in these mice until 24 weeks after infection.

Since these facts are similar to our early observations in human leprosy, the suppression of specific immune response is discussed in relation to antileprous immunity in human and experimental murine leprosy.—(*Adapted from* Authors' Summary)

Kawaguchi, Y., Matsuoka, M., Sushida, K. and Tanemura, M. Susceptibility to *Mycobacterium avium* of C3H/He mice. Jpn. J. Lepr. **50** (1981) 128–134. (in Japanese)

C3H/He strain mice, approximately six weeks of age, were inoculated intraperitoneally with 0.5 mg of *Mycobacterium avium*, strain Kirchberg. The inoculum was prepared by the grinding method from a 13-day culture of *M. avium* grown on 1% Ogawa's medium. The susceptibility of these mice to the bacilli was evaluated mainly by the average survival time of experimental mice and their visceral lesions.

The susceptibility of mice of five inbred strains, C3H, C57BL/6, DDD, BALB/c and KK, was also examined by the same manner mentioned above, as controls.

Clear differences in the host resistance to *M. avium* could be demonstrated in these strains, markedly between C3H and the other strains, including C3H/He. Average survival time and grade of visceral lesions of C3H/He mice were intermediate to those observed in C3H and the other four strains, but far different from those of C3H strain.—Authors' Summary

Krahenbuhl, J. L., Humphries, R. C. and Henika, P. C. Effects of *Propionibacterium acnes* treatment on the course of *Mycobacterium leprae* infection in mice. Infect. Immun. **37** (1982) 183–188.

Studies were carried out to determine the effects of treatment with killed suspensions of *Propionibacterium acnes* (formerly designated *Corynebacterium parvum*) on the course of *Mycobacterium leprae* infection in mice. Systemic (intravenous or intraperitoneal) treatment with *P. acnes* failed to significantly alter the growth of *M. leprae* in the mouse foot pad. In contrast, injections of *P. acnes* directly into the infected foot pad markedly inhibited the growth of the leprosy bacilli regardless of whether the local treatments were administered before

infection or three months after infection with *M. leprae*. The effects of local treatment with *P. acnes* appeared to be bactericidal and not merely bacteriostatic. Clearance of the organism from the tissues was not enhanced by *P. acnes* treatment.—Authors' Summary

Mor, N., Lutsky, I. and Levy, L. Response in distant lymph nodes of mice to infection in the hind foot pad with *Mycobacterium marinum*. Infect. Immun. **28** (1980) 225–229.

In an attempt to demonstrate the importance of the popliteal lymph node in limiting the progress of infection with *Mycobacterium marinum* in the hind foot pads of C57BL mice, such infections were studied in mice subjected to popliteal or popliteal and inguinal adenectomies. In the absence of the popliteal node, the foot pad infection was only slightly enhanced compared with infections of sham-operated control mice; the inguinal node was found to be greatly enlarged and appeared to have substituted for the absent popliteal node. In the absence of both popliteal and inguinal nodes, the disease process in the foot pads was again only slightly enhanced, and the axillary node appeared to have enlarged greatly and to have functionally replaced the missing, more proximate nodes. In additional experiments, mice subjected to adenectomy only on one side and injected in that hind foot pad with phytohemagglutinin or India ink demonstrated hypertrophy or deposition of carbon particles in the more distant node only on the side of the injection. Thus, there appear to be rather direct functional connections among popliteal, inguinal, and axillary nodes that do not depend on blood circulation.—Authors' Summary

Mor, N., Lutsky, I. and Levy, L. Response in the hind foot pad and popliteal lymph node of C57BL mice to infection with *Mycobacterium marinum*. Isr. J. Med. Sci. **17** (1980) 236–244.

C57BL mice inoculated in the hind foot pads with 5×10^3 viable *Mycobacterium marinum* developed a localized disease process, characterized by swelling of the foot and increases in the number of acid-fast bacilli and colony-forming units recovered. These changes became maximal 10–14 days after inoculation and then decreased in intensity. An acute inflammatory response appeared in the hind foot pad during the first 24 hr and increased in intensity during the next few days. By seven days after inoculation, the polymorphonuclear leukocytes had been largely replaced by lymphocytes and macrophages which led, during the next two weeks, to the extensive formation of granulomas. Epithelioid granulomas developed after at least 90% of the organisms had been killed. Simultaneously the popliteal lymph node increased greatly in size due to hyperplasia of the paracortical area, which contained a large number of pyroninophilic cells, and packing of sinusoids with small lymphocytes. Well-formed epithelioid granulomas containing acid-fast bacilli developed in the popliteal node. A small number of viable bacilli were found in both the hind foot pad and the popliteal node 18 months after inoculation; this was accompanied by solid resistance to secondary challenge.—Authors' Summary

Mori, T., and Nyein, M. Study of growth factor for *Mycobacterium lepraemurium* grown in the Ogawa yolk medium. II. Egg yolk protein fraction and effect of reducing reagents. Jpn. J. Lepr. **50** (1981) 105–115.

One of the growth factors of *Mycobacterium lepraemurium* in 1% Ogawa yolk medium might be a reducing action of the yolk protein fraction. Egg white medium containing the water insoluble fraction of egg yolk did not permit the good growth of *M. lepraemurium*. However, growth of *M. lepraemurium* similar to that seen with the full egg yolk medium was seen on egg white medium supplemented with a high molecular weight fraction of a boiling water extract of egg yolk. This extract did not accelerate the growth of *M. lepraemurium* on minimal medium. Since the water insoluble fraction of egg yolk was a high molecular weight lipoprotein particle, purification of this growth factor could not be achieved. Thioglycolate, reduced glutathione, or cysteine accelerated the growth of *M. lepraemurium* on Kirchner agar medium containing 10% bovine serum.—Authors' Summary

Ng, H., Welch, T. M., Baras, M. and Levy, L. Protection of mice by intraperitoneal vaccination against challenge in the foot pad with *Mycobacterium marinum*. Isr. J. Med. Sci. **16** (1980) 849–852.

In a study of local infection of mice with *Mycobacterium marinum*, heat-killed *M. marinum* suspended either in Hanks' balanced salt solution or in Freund's incomplete adjuvant was administered i.p. to BALB/c mice. The mice were challenged in the hind foot pad 3, 7, or 14 days thereafter with 5×10^3 viable *M. marinum*. At every time interval, killed *M. marinum* in the saline medium conferred modest protection against the challenge infection; whereas the antigen suspended in adjuvant conferred protection only when the challenge was administered 14 days after vaccination. Freund's incomplete adjuvant appeared to enhance the infection and to minimize the immune response to the antigen.—Authors' Summary

Ng, H., Welch, T. M. and Levy, L. Survival of BALB/c mice after intravenous infection with *Mycobacterium marinum*. Isr. J. Med. Sci. **16** (1980) 452–455.

In a search for a simple technique by which to study the disease of mice that follows infection with *Mycobacterium marinum*, survival of BALB/c mice after i.v. inoculation of *M. marinum* was measured. Length of survival was inversely proportional to the number of viable organisms in the inoculum, and was greater in weanling than in yearling mice. Prior infection with *M. marinum* in a hind foot pad at least two weeks before i.v. challenge with the same organism conferred protection against the challenge.—Authors' Summary

Packchanian, E., Emery, R., MacDonald, E. M. and Rigdon, R. H. Experimental leprosy with *Mycobacterium lepraemurium* in hairless mice (*Mus musculus*). Trans. R. Soc. Trop. Med. Hyg. **76** (1982) 183–186.

"... The results of this study have demonstrated that the hairless mouse, *Mus musculus*, is a suitable laboratory animal for studying experimental cutaneous leprosy. The skin lesions of murine leprosy are reproducible in both male and female, in young and adult hairless mice. In addition, the life-span of hairless *Mus musculus*, which is over three years, allowed ample time for studying the disease process ..."—(*From* Trop. Dis. Bull.)

Preston, P. M. Macrophages and protective immunity in *Mycobacterium lepraemurium* infections in a 'resistant' (C57Bl) and a 'susceptible' (BALB/c) mouse strain. Clin. Exp. Immunol. **47** (1982) 243–252.

The progressive low resistance form of *M. lepraemurium* infection in BALB/c mice and the more benign form of infection in C57Bl mice provided appropriate models for analyzing the role of macrophages in the spectrum of leprosy in man. Although C57Bl mice were more resistant to both primary and challenge infections than BALB/c mice, peritoneal macrophages from infected mice of both strains were bacteriostatic *in vitro*. However, a diffusion chamber technique demonstrated that macrophages of BALB/c mice were usually less effective in controlling mycobacterial multiplication *in vivo* than those of C57Bl mice. This technique also revealed two diffusible factors in infected mice of both strains; one able to activate, the other able to suppress macrophage anti-mycobacterial activity. In C57Bl mice, the macrophage activating factor was apparently dominant; in BALB/c mice, the macrophage suppressor factor seemed to play the major role.—Author's Summary

Venkataramaniah, H. N., Harikrishnan, S., Balakrishnan, S. and Bhatia, V. N. A comparison of the skin scrape and skin biopsy methods in mouse foot pad experiments with *M. leprae*. Lepr. India **54** (1982) 59–61.

During the years 1977–80, a total of 98 batches of foot pad experiments with *M. leprae* were performed, 55 with skin-scrape suspension and 43 with regular skin biopsy suspensions. The mean BI of the patients included in the two groups of the study was 2.69 and 2.41, respectively. The mean bacillary count/ml of suspension was 2.3×10^6 and 1.8×10^6, respectively. The percentages of "takes" in mouse foot pad were 87.3 and 83.5, respectively.—Authors' Summary

Epidemiology and Prevention

Bharadwaj, V. P., Ramu, G. and Desikan, K. V. A preliminary report on sub-clinical infection in leprosy. Lepr. India **54** (1982) 220–227.

The present paper describes the results of the lepromin (Dharmendra) test and the FLA-ABS test administered simultaneously in contacts of leprosy patients. The aims of the present study were a) to measure subclinical infection in household contacts, and b) identify those who are at risk of getting the disease. A total of 138 contact children of leprosy cases were studied. Overall, 48% were lepromin positive and 52% were lepromin negative. Thirty-two percent of the lepromin positive contact children were FLA-ABS negative. Seventy-eight percent of the lepromin negative contact children were FLA-ABS positive. According to FLA-ABS test results, sub-clinical infection was more common among contacts of multibacillary cases than among contacts of paucibacillary cases. A negative lepromin test and a positive FLA-ABS test indicates a high risk of getting leprosy and such contacts may be candidates for developing serious forms of the disease.—(*From the* article)

Dharmendra. Detection of sub-clinical infection in leprosy. (Editorial) Lep. India **54** (1982) 193–207.

The author has succinctly reviewed the bacteriological, epidemiological, and immunological evidence for the existence of sub-clinical infection in contacts of leprosy patients. Acid-fast bacilli were found in skin smears of a number of healthy contacts of lepromatous cases and, to a lesser extent, in contacts of nonlepromatous cases in 1949. Epidemiologic evidence was found in the 1970s that in a leprosy endemic area, healthy individuals who harbored acid-fast bacilli in their skin were almost six-times more likely to develop leprosy within two years than bacteriologically negative individuals. The available skin tests and serological tests for leprosy are reviewed and the significance of their results are discussed. (39 references)—(*From the* Editorial)

Dominguez, V. M., Barbajose, P. G., Gyi, M. M., Tamondong, C. T., Sundaresan, T., Bechelli, L. M., Lwin, K., Sansarricq, H., Water, J. and Noussitou, F. M. Epidemiological information on leprosy in the Singu area of Upper Burma. Bull. WHO **58** (1980) 81–89.

In the course of a WHO trial designed to evaluate the possible protective action of BCG vaccine against leprosy, a longitudinal epidemiological study of the whole population was carried out in an area of very high endemicity in Burma from 1964 to 1976. Two mass surveys of the whole population with an interval of four years and annual re-examination of the 28,000 children (0–14 years) in the BCG trial were carried out. The data collected yielded important information about general prevalence and yearly incidence of the disease as well as on sex, age, and classification of cases. The general prevalence rate declined from 32.6/1000 in the first survey to 25.2/1000 in the second. The number of cases among males was significantly higher than among females. Incidence rate among contacts of already known cases was 9.8/1000 person-years. The estimated yearly incidence among non-contacts was 5.9/1000. Prevalence rates reached a peak in the 20–39-year age group. The prevalence rate of multibacillary patients also reached a peak in the same age bracket. It is stressed that a further period of epidemiological surveillance will be essential in order to have a correct estimate of the expected number of new infections, especially multibacillary cases, in the 20–39-year group. The value of this information is considered unique for planning and programming of future control activites.—Authors' Summary

Hogerzeil, L. M. and Reddy, R. K. General health education as the main approach to leprosy control, Dichpalli, India. Lepr. Rev. **53** (1982) 195–199.

Leprosy control in an integrated community health project (CHP) and in a conventional survey, education, treatment (SET) program are compared over a period of five years.

In the CHP priority was given to intensive, continuous health education on various subjects, including leprosy, by mainly illiterate village health workers (VHW), 1/1000 population.

In the SET program the emphasis was on house-to-house survey for leprosy patients only by well educated paramedical workers, 1/20,000 population.

Case finding in the SET was better than in the CHP. However, while the number of new patients in the SET remained fairly constant over the years, it more than doubled in the CHP. Case holding in the SET gradually increased to 64% of the registered patients receiving regular treatment; while in the CHP the corresponding figure rose to 90%.

The integrated approach with the emphasis on health education seems to lead to a better quality contact between the VHW and the leprosy patient. Supervised combined therapy of all patients, tuberculoid and lepromatous, in accordance with the latest principles is now a distinct possibility.—(Authors' Summary)

Izumi, S., Sugiyama, K., Matsumoto, Y. and Ohkawa, S. Analysis of the immunogenetic background of Japanese leprosy patients by the HLA system. Vox Sang. **42** (1982) 243–247.

Tow hundred ninety-five lepromatous and 74 tuberculoid leprosy patients were typed for HLA-A, -B and -C and compared to 110 healthy controls. It was found that frequency of HLA-B7 was significantly high and that of Bw54 was significantly low in lepromatous leprosy. HLA-DR and MT types were investigated in 84 lepromatous and 28 tuberculoid patients and compared to 55 controls. Both lepromatous and tuberculoid patients showed a marked increase in DR2 frequency. The relative risk is 8.7% and 5.9%, respectively. Lepromatous leprosy showed an increase in frequency of MT1 and decreases in those of DRw9 and MT3.—(Authors' Summary)

Levis, W. R., Schuman, J. S., Friedman, S. M. and Newfield, S. A. An epidemiologic evaluation of leprosy in New York City. JAMA **247** (1982) 3221–3226.

Leprosy is a transmissible disease that is propagated from human to human. At the U.S. Public Health Service Hospital, New York City, the number of new leprosy cases per year during the 1970s was about three times greater than in the previous decade. This review of our 100 most recent leprosy patients shows that 60% were of the lepromatous and borderline lepromatous type. Ninety-nine of the patients were foreign born, originating in more than 26 countries. This emphasizes that, at this time, the leprosy problem in New York City is almost exclusively a reflection of immigration patterns. The majority of the patients were asymptomatic at the time of entering the United States. The average latent period from entering the United States until onset of symptoms was 4.8 years, with a range of 0 to 38 years. These figures emphasize the need for physicians to be aware that leprosy can occur as long as five to 40 years after emigration from endemic areas. For all types of leprosy, the average lag from the onset of symptoms to the time of diagnosis was 29.0 months (range, 0 to 245 months). Our experience indicates that a program of urban leprosy treatment using available drugs and supportive care is feasible.—Authors' Summary

McNulty, J. C. Leprosy amongst Aboriginals. (Letter to Editor) Med. J. Aust. **1** (1982) 60.

With regard to the incidence of leprosy in the Pilbara, the 1981 figure is 0.3810/1000 Aboriginals. With regard to prevalence, the removal of persons from the Hansen's register occurs only on death or permanent removal from the state, so that the prevalence rate for Pilbara of 3.4286/1000 Aboriginals does not represent an uncontrolled situation but the attention given to cases found.

It is recognized that leprosy generally shortens the expectation of life. Western Australia was the first state to produce life tables for Aboriginals. The life expectancy at birth of Aboriginals in Western Australia in 1976 was 63 years for males and 66 years for females. Since the Aboriginal infant mortality rate has improved from 45.6/1000 in 1976 to 29.4/1000 in 1979, it is reasonable to assume that life expectancy has also improved since 1976. Aboriginals therefore live

longer and those with leprosy also live to a good age. (In fact three of the Aboriginals in the Pilbara with Hansen's disease are over 80 years of age.)—(*From the* Letter to the Editor)

Rao, P. S. S., Prasad, K. R. and Bai, K. I. A study of leprosy among urban and rural school children of Andhra Pradesh. Lepr. India **54** (1982) 100–109.

The field survey among school children in Tirupati town in Chittoor District and Kambadur village in Anantapur District has revealed prevalence rates of clinical cases of leprosy 23.0/1000 and 22.9/1000, respectively. The study included testing with lepromin A and the results of the test in relation to variables like age, nutritional status, BCG vaccination, etc., have been presented. The importance of school surveys in leprosy control programs has been highlighted.—Authors' Summary

Saikawa, K. The epidemiological phenomenon on decreasing tendency of leprosy disease. Jpn. J. Lepr. **50** (1981) 99–104. (in Japanese)

Epidemiologic studies of decreasing leprosy prevalence rates have been done by many leprologists.

An epidemiological field pilot study has been done in Okinawa on the decreasing leprosy incidence rate. Okinawa was the most severe leprosy endemic area in Japan, and in 1967 the leprosy incidence rate was 0.181/1000. Recently the situation has very much improved and the incidence rate was 0.017/1000 in 1980. Leprosy out-patient treatment has been in operation in Okinawa since in 1961, and it has been easy to collect data on newly detected patients. The following results were obtained:

1) The leprosy incidence rate, lepromatous incidence rate, child incidence rate, and child ratio (under 14 years old) all showed a decreasing tendency. The child incidence rate and the child ratio were decreasing at a faster pace than the leprosy incidence rate.

2) The lepromatous ratio and proportion of aged patients (over 65 years old) increased during this time.

3) During this time, the ratio of male to female patients declined, especially among children.

4) The proportion of childhood cases (falling) crossed the proportion of aged patients (rising) during this time period. This was a striking finding and, as has been previously noted, suggests a declining leprosy incidence rate.

5) During this time, the peak of the onset age curve moved from the younger group to the older group.—(*Adapted from* the Author's Summary)

Sehgal, V. N., Koranne, R. V., Sharma, A. K., Misra, S. and Jain, R. K. Age at onset of leprosy (an analytic data from Northern India). Lepr. India **54** (1982) 332–337.

Very little information is available from northern India about various intriguing facets of epidemiology of leprosy. Age at onset is a very important aspect of the epidemiology of the disease process. In the present study analytic data of the patients from northern India is presented. The mean age at onset of leprosy in males was 31.49 and in females, 29.43. The mean age at onset for N, N?L and L types was 30.14, 30.12 and 34.13, respectively. The data compared well with those of earlier series.—Authors' Summary

Unwanted import on the rise: Leprosy. Med. World News, November 23, 1981, 80.

Leprosy cases detected in the U.S.—almost all imported—have more than tripled in the past decade, rising from 50 or 60 a year to at least 200. Since immigrants from areas in the Caribbean, South America, Africa, and Asia, where leprosy is endemic, are finding new homes throughout this country, many physicians may be seeing their first case.

The infection—now called Hansen's disease to avoid the old stigma—can escape detection by immigration health officers because of its long latent stage. The disease will probably not spread in the U.S. and Canada, however, because of the population's high living standards and lack of genetic susceptibility. But it could become a medium-level problem among immigrants.

Despite current phasing out of the U.S.

Public Health Service hospital system, the Carville Louisiana, U.S.A., center will remain open. Patients elsewhere will probably be eligible to receive care from regional facilities under PHS-funded contracts.—(*From* the article)

Rehabilitation

Kulkarni, V. N. and Mehta, J. M. Observations on peg-prosthesis in leprosy. Lepr. India **54** (1982) 110–116.

Three leprosy patients with peg-prosthesis were studied in detail. It was found that there were several disadvantages of this type of prosthesis. However, its application in a rural situation has some merits and, with some suggested modifications, it could be adopted with better results.—Authors' Summary

Kumar, A. and Anbalagan, M. Illness and service utilization behaviours of leprosy patients. Lepr. India **54** (1982) 338–347.

Two hundred twenty-five adult leprosy patients attending the Central Leprosy Teaching and Research Institute, Chingleput, India, were interviewed to study their illness and medical agency utilization behaviors. Almost all patients perceived their disease as leprosy but 71.50% did not know how they got it; 10%–11% did not reveal the disease to their family for fear of rejection. The time lag between first suspicion and medical consultation was one year or more in 48% of cases. For treatment of leprosy, 36%–38% of patients consulted private practitioners and general hospitals at one time or another; 42.6% of patients changed three or more medical agencies for treatment. On an average the patients had taken 62.39% of expected treatment; 41% of patients were not aware of the name of drug (DDS) they were taking; 44% of patients had tried home remedies. Most of the patients preferred to take treatment at leprosy referral hospitals.—Authors' Summary

Pina, N. C. and Manzi, R. O. Rehabilitacion en lepra; aspectos socioantropopologicos. (Rehabilitation in leprosy; socio-anthropological aspects.) Temas de Leprol. **69** (1981) 5–40.

El esfuerzo realizado para el relevamiento y análisis de los datos ha sido ampliamente compensado con la satisfacción que no ha producido el haber podido tomar contacto con el problema de la lepra a través de un diálogo que en todos los casos—pese a lo conflictivo del tema—fue franco y en el cual el interlocutor participaba con interés y buena disposición.

Como conclusiones podemos afirmar que el conocimiento de los distintos grupos encuestados varía en función de la distancia que mantienen con la enfermedad. Así observamos cómo los pacientes tienen, en general, un conocimiento más exacto de las características de la enfermedad, su evolución y su pronóstico, que en muchos casos es superior al del personal paramédico de dermatología. Son también los pacientes los que han internalizado mejor los nuevos conceptos en cuanto a control de la enfermedad.

También se notan diferencias cuando comparamos los conocimientos de los médicos dermatológicos y el de los médicos clínicos y el de los distintos grupos de paramédicos. La diferencia siempre está a favor del personal asistencial de Dermatología.

La falta de información de la población de centro urbano, representada en este caso por Cañuelas, nos alerta acerca de todas las dificultades que tenemos que vencer para cambiar la conceptualización e imagen de la enfermedad. Las manifestaciones de los habitantes de Rodríguez, confirmada por los pacientes internados, constituyen un claro exponente de los efectos de una acción permanente. La circulación continua de la información, ya sea en forma oral o de su materialización en la presencia del enfermo ha ayudado a corregir viejas ideas. Está claro que el proceso no está aún acabado, pero se pueden predecir los resultados si estas acciones espontaneas se encuadran en la planificación y coordinación de los sectores interesados.

Por otra parte también los datos nos revelan el interés de la población en poseer la información necesaria para prevenir la enfermedad, a la vez que nos señala la escuela cómo el lugar más indicado para darla.

Queda claro además lo innecesario de un cambio de nombre de la enfermedad para corregir el prejuicio cuando la información adecuada impide la formación de preconceptos.

La actitud hacia el enfermo de lepra así como todas las conductas defensivas que adopta el paciente, no son más que otras manifestaciones de la falta de información que no sólo alcanza al enfermo sino también a su familia.

Observamos también cómo la población encuestada traduce las mismas contradicciones que plantea el conocimiento actual y cómo la elaboración personal o la experiencia individual ocupan el vacío que deja la explicación científica.

La conducta de los pacientes, en cuanto al control de su enfermedad, puede considerarse adecuada y revela una actitud positiva hacia la enfermedad y una confianza en la Medicina que facilita la labor médica y hace posible las acciones preventivas.

Por todo esto consideramos que las condiciones para iniciar acciones educativas referidas a rehabilitación, están dadas.

Una moderna concepción de la rehabilitación no se efectiviza solamente con la incorporación de técnicas novedosas o con la creación de un nuevo lenguaje que oculte o disfrace viejas ideas y comportamientos. Es indispensable integrar nuevos elementos al sistema vigente, esto es: el paciente como participante activo del proceso rehabilitación y equipos interdisciplinarios que con instrumentos adecuados hagan posible el tratamiento integral del enfermo, considerando sus aspectos físicos, psíquicos y socioculturales.—(*From the* article)

Malaviya, G. N. and Ramu, G. Role of surgical decompression in ulnar neuritis of leprosy. Lepr. India **54** (1982) 287–302.

The present study was undertaken to evaluate the effect of neurolysis in relieving the pain of acute painful neuritis and assess its effect on the sensory motor deficit.

Thirty-eight ulnar nerves were operated on and followed up for 8 to 125 weeks. Following surgery, relief from pain was gratifying. However the pain recurred in cases of lepromatous leprosy in subsequent episodes of ENL reaction.

Sensory recovery was appreciable and occurred within eight weeks. Four cases had 75% recovery; five had 50%–75% recovery and 11 cases had up to 50% recovery. Motor recovery took a longer time to appear. Proximal supplied muscles recovered first followed by smaller muscles. In most cases further deterioration of muscle power was prevented. Only three cases deteriorated. Recovery was more pronounced in LL cases. Patients with shorter duration of acute symptoms and history of smaller number of attacks of acute painful neuritis showed a higher incidence and better grade of recovery.—Authors' Summary

Prasad, S. B. Surgical problems of acute onset in leprosy patients and their management in leprosy control programmes. J. Indian Med. Assoc. **76** (1981) 168–172.

Out of 301 patients of leprosy deformities (30% of total patients), 101 cases presenting with surgical problems of acute onset (10% of total patients: 33% of deformity cases) were selected from a closed community of Leprosy Control Unit, Raxaul, India. They were managed with simple preventive and curative means. The result showed a very good rate and extent of recovery; none of them went to chronic stage of deformity. The statistical data of patients selected, presentation of acute surgical problems, and their management have been discussed. In a control program, the role of such preventive measures carries paramount importance to arrest the development of various crippling deformities associated with leprosy. An emphasis on the management of such acute problems must be given during the training period to the persons engaged in a leprosy control program.—Author's Summary

Sebille, A., Saint-André, P. and Hugelin, A. Accélération de la réinnervation musculaire par l'isaxonine; Mise en évidence électrophysiologique au cours des neuropathies hanséniennes. (Acceleration by isaxonine of muscle reinnervation; Elec-

trophysiological demonstration in leprotic neuropathy.) Nouv. Presse Med. **11** (1982) 1278–1280. (in French)

On a model of compressive human neuropathy—leprous neuropathy occurring below an osteoligamentary canal following a process of sclerosis—a double-blind survey of isaxonine versus a placebo was undertaken after matching of patients to obtain similar pairs. After four months of treatment with isaxonine, the electrophysiological tests (EMG of the anterior tibialis and of the abductor digiti minimi muscle) showed a very significant improvement in the graphs of patients receiving the active agent, as compared to a lack of improvement, even an aggravation, for those patients receiving the placebo. It may thus be concluded that muscular reinnervation has occurred, either by sprouting of the remaining healthy fibers or by regeneration of the damaged axons, or by both phenomena simultaneously.—Authors' Summary

Vyas, G. K., Dudani, I. U. and Chaudhary, R. C. A sociological study of leprosy cases in the Gandhi Kusth Ashram, Jodhpur (Rajasthan). Lepr. India **54** (1982) 324–331.

A sociological study was carried out in respondents of a Lepers Colony (sic) (Gandhi Kusth Ashram), Jodhpur, India. An attempt was made to study the knowledge about causation of leprosy, age at onset, and treatment. The reason for leaving their original place of origin (south India) was enquired. A majority (95.2%) of patients were Hindus, had onset of leprosy in the age group of below 20 years to 30 years (80.94%), and had a literacy rate of only 6.3%. A history of contact with a case of leprosy could be traced in 38% but within the family only in 11.9%. The infection as a cause of leprosy was recognized only by 3.57% patients but a majority had no idea about etiology (70.24%) or thought it to be due to punishment for past sins (3.57%) or due to supernatural causation (1.19%). Most of them (70.2%) left home for fear of losing family prestige and to hide the disease (25.00%) or hatred of other family members (4.76%).—Authors' Summary

Other Mycobacterial Diseases and Related Entities

Casal, M. and Rodriguez, F. *In vitro* susceptibility of *Mycobacterium fortuitum* and *Mycobacterium chelonei* to cefoxitin. Tubercle **63** (1982) 125–127.

The *in vitro* action of cefoxitin against 63 strains of *Mycobacterium fortuitum* and 20 strains of *M. chelonei* was investigated. At a drug concentration of 16 μg/ml, 48% of strains of *M. fortuitum* and 10% of strains of *M. chelonei* were inhibited.—Authors' Summary

Gatner, E. M. S., Msibi, V. and Dauth, J. Circulating immunoglobulin levels in patients with pulmonary tuberculosis with special reference to IgE. Tubercle **63** (1982) 113–117.

This study has demonstrated high levels of circulating IgE in a group of patients with pulmonary tuberculosis compared with a control group. There was little or no specific binding of circulating IgE to *Mycobacterium tuberculosis* but when the serum was heated to 56°C for 1 hr, 5/20 of the patients investigated showed appreciable levels of binding. It is suggested that the IgE which binds to *M. tuberculosis* exists in a heat-labile complex with an anti-IgE antibody and that this complex formation may represent a protective host mechanism.—Authors' Summary

Gatner, E. M. S. and Anderson, R. Immune responses and immuno-stimulation in tuberculosis therapy. S. Afr. Med. J. **61** (1982) 707–710.

Despite a reasonably extensive literature on cellular and humoral immune responses in tuberculous disease, abnormalities tend to be secondary rather than predisposing to disease. No discrete immune deficiency or failure, which would explain the progres-

sion from non-infection to infection with *Mycobacterium tuberculosis* to tuberculous disease, has been identified. There is evidence that tuberculous disease occurs in a spectrum, analogous to leprosy, and it would seem that if immunostimulants, as adjuncts to standard therapy, are to be of any value in the treatment of tuberculosis, they should be used for non-reactive tuberculosis patients. The range of immunostimulants currently available tends to be indiscriminate in action and their targets in tuberculous disease largely uncertain; their role in therapy is discussed.—Authors' Summary

Kadival, G. V., Samuel, A. M., Virdi, B. S., Kale, R. N. and Ganatra, R. D. Radioimmunoassay of tuberculous antigen. Indian J. Med. Res. **75** (1982) 765–770.

A radioimmunoassay using a cell sonicate antigen of H37Rv strain of *Mycobacterium tuberculosis* has been standardized. The assay is sensitive to detect 1×10^3 organisms/ml or the equivalent of 1 ng/ml of sonicate antigen. It is specific in the detection of H37Rv and *M. bovis* with negligible cross reactivity against other mycobacteria. Antigen could be detected in biological samples like sputum of patients with pulmonary tuberculosis in both smear positive as well as those which were only culture positive later. This test can be used for diagnosis of active tuberculosis in systemic infections caused by *M. tuberculosis*.—Authors' Summary

Khuller, G. K., Malik, U. and Subrahmanyam, D. Immunological studies with sulpholipids of mycobacteria. Tubercule **63** (1982) 107–111.

Antibodies to sulfolipids of mycobacteria were produced in rabbits when injected as sulfolipid-MBSA complexes and were detected by kaolin agglutination and double diffusion techniques. Sulfolipid antibodies did not cross react with any other lipids of mycobacteria except cord-factor. The antigenicity of sulfolipids appears to be due to α-D-trehalose and sulfate groups. Guinea pigs immunized with sulfolipid-MBSA complexes showed partial protection against tuberculous infection with *Mycobacterium tuberculosis* H37Rv, as revealed by mortality rate and score of lesions.—Authors' Summary

Mirza, Z. Immune status in pulmonary tuberculosis patients. Pak. J. Med. Res. **20** (1981) 81–90.

Cell-mediated immunity was shown to be depressed in a group of 47 adults with pulmonary tuberculosis. Of 20 untreated patients, 65% failed to become sensitized to dinitrochlorobenzene (DNCB). Corresponding figures for 16 and 11 patients treated for 3–6 months and for more than 1 year, respectively, were 56.3% and 27.3%. None of a control group of 18 healthy subjects failed to become sensitized to DNCB. This finding contrasts with recall reactions to purified protein derivative (PPD) where only 10% of untreated patients failed to give a positive reaction. None of the treated patients or control group failed to respond to PPD. Untreated patients and those treated for only 3–6 months had lower total peripheral blood counts for T lymphocytes than the other groups but no tests of T cell function *in vitro* were performed.—K. C. Watson (*From* Trop. Dis. Bull.)

Reich, M., Affronti, L. F. and Wright, G. L., Jr. Isolation and partial characterization of the most immunologically reactive antigen from *Mycobacterium tuberculosis* H37Ra culture filtrate. Tubercle **63** (1982) 99–106.

The culture filtrate of *Mycobacterium tuberculosis* H37Ra was fractionated by ammonium sulfate precipitation, diethyl aminoethyl (DEAE) cellulose-Sephadex A-50 column chromatography, preparative isoelectric focusing and polyacrylamide gel electrophoresis to isolate the most antigenic tuberculoprotein. One protein, designated P2, was isolated and determined by immunodiffusion to be the most immunologically reactive antigen present in H37Ra culture filtrate. This protein had a molecular weight of about 22,000, a sedimentation constant of 2.2S and was present in Seibert's A, B, and C proteins.—Authors' Summary

Taneja, R., Malik, U. and Khuller, G. K. Effect of growth temperature and exogenous fatty acids on the lipid composition

of *Mycobacterium phlei*. Indian J. Med. Res. **75** (1982) 648–653.

Low growth temperature and supplementation of unsaturated fatty acids to the medium of *Mycobacterium phlei* resulted in an increase in total lipids and acylglycerols, while the effect on total phospholipids varied. Among the individual components, phosphatidylinositolmannosides were observed to decrease whereas significant increases were noted in the contents of phosphatidylethanolamine and di- and triacylglycerols.—Authors' Summary

Tuberculosis control: A world review. Weekly Epidemiol. Rec. **56** (1981) 393–396. (in English and French)

This is a review of the tuberculosis problem throughout the world. The epidemiological indices considered to be most relevant are the age-specific prevalence of persons excreting tubercle bacilli demonstrated by direct smear examination and the tuberculin reactor rate which indicates risk of infection. Both indices have to be determined by mass surveys.

The information obtained so far is insufficient to cover the whole world, but it indicates large differences between developed and developing countries. The disease has long been on the decline in the former but such a decline is scarcely observable in the latter. In developed countries tuberculosis is becoming a disease of old age, and with the adequate treatment now available it is no longer a serious public health problem. In many developing countries it remains a disease of both young and old.

The risk of infection at a specific age (such as at school entry) is a good indicator of the trend of the disease, and it has been shown that there is an almost constant ratio between the risk of infection and the incidence of smear-positive tuberculosis. In developing countries there is evidence that every 1% incidence of infection corresponds to 50 new cases of sputum-positive pulmonary tuberculosis per year/100,000 population.

In the developed countries the annual decline in the reactor rate (risk of infection) is about 12%, which means that it halves every five or six years. In the developing countries the decline is minimal.

Contrary to previously accepted belief, it was shown that when the risk of infection declines sharply the risk of tuberculous disease in persons already infected also declines. This finding led to the conclusion that unless the risk of infection is low new cases of tuberculosis arise among those already infected, predominantly as a result of reinfection.

Because of lack of uniformity in the criteria for diagnosis and reporting, comparisons between different countries cannot be made, and moreover mortality figures are not reliable. Many patients dying *with* tuberculosis are notified as dying *of* tuberculosis. Morbidity and mortality statistics are therefore not suitable epidemiological indices.

Available statistics show that between 1965 and 1979 over 1 million new cases of tuberculosis were reported throughout the world; this must be only a small fraction of the true number. Reported deaths from tuberculosis fell from 178,213 in 1965 to 53,545 in 1979. Decreases reported were mainly in the developed countries. The figures from the developing countries mean little, and the true number of deaths must be many times greater than that reported.—H. G. Calwell (*From* Trop. Dis. Bull.)