

Abstracts

1. GODAL, T., MYRVANG, B., STANFORD, J.-L. & SAMUEL, DOROTHY R. Recent Advances in the Immunology of Leprosy with Special Reference to New Approaches in Immunoprophylaxis. *Bull. Inst. Pasteur*, 1974, 273

This long paper makes exciting reading. The earlier sections describe clearly, concisely and comprehensively the recent work which has placed our understanding of the immunology of leprosy on firm foundations, given meaning to the clinical and pathological spectrum of the disease and its complications, and provided a fresh approach to its epidemiology. For this alone the paper is very valuable, but in substantial concluding sections on Immunotherapy and Immunoprophylaxis important new work is described.

This concentrates particularly on the search for a cross-reactive mycobacterium inducing protection against *Myco. leprae*. Screening of 20 different mycobacterial strains indicated that while BCG had some action, the vole bacillus (*Myco. microti*) is antigenically more closely related to *Myco. leprae* than is BCG, its cross reactivity to *Myco. leprae* being both at a higher level and more persistent. Furthermore, in rabbits this reactivity could be increased three to four fold if *Myco. duvalii* was mixed with BCG or the vole bacillus. A sphere of study of immediate importance in the development of a vaccine for prophylactic use in leprosy is thus opened up. Reference is also made to evidence which suggests that the addition of *Myco. leprae* to BCG in rabbits can provoke an *Myco. leprae* specific LTT response which is not achieved with BCG or *Myco. leprae* alone. Clearly we are on the threshold of an important advance in the immunoprophylaxis of leprosy.

T. F. Davey

2. BROWNE, S. G. Some Aspects of the History of Leprosy: The Leprosie of Yesterday. *Proc. R. Soc. Med.*, 1975, v. 68, 485.

This masterly paper, read by invitation before the Royal Society of Medicine, first gives a concise account of early records of leprosy in Asia and Africa, proceeds to trace the spread of the disease by soldiers, sailors and merchants through the Mediterranean Collateral and into Europe, and then concentrates on the history of the disease in England and Scotland. An impressive array of records is sifted with great refinement, and a picture of leprosy emerges which demolishes several myths and is authenticated by the sound scholarship and great experience of the author. The text is enlivened by some interesting quotations. It is impossible briefly to summarize the content of this paper, which itself should be read and treasured by leprologists everywhere.

T. F. Davey

The following Abstracts are reprinted, with permission, from *Tropical Diseases Bulletin*, 1975, May to July.

3. HASSELBLAD, O. W. Psycho-social aspects of leprosy. *Bull. Pan. Am. Hlth Org.*, 1974, v. 8, No. 4, 283-8.

“ . . . While there are no certain solutions for the psycho-social problems of leprosy, a number of positive steps have proven productive. These include a variety of measures to assist the

patient's development of a sound mental attitude during diagnosis; a public health approach to leprosy management that permits the person being treated to remain at home; treatment of leprosy cases at general medical facilities rather than special facilities; accurate and carefully thought-out programs of public health education; and health education of the patient and his family aimed at prevention and treatment of the adverse psychological effects of his condition."

4. NEBOUT, M. Observation d'un cas de Lèpre tuberculoïde nodulaire consécutive à des scarifications rituelles. [Report of a case of nodular tuberculoid leprosy following ritual scarification.] *Méd. Afr. Noire*, 1974, v. 21, No. 11, 867-70. English summary.

In 1945, three years after ritual scarifications were made with an unsterile metal instrument on a male aged 15 years of the Central African Republic, large nodules began to appear in the resulting cheloid scars on the face. Nearly 25 years later, similar nodules developed in a symmetrical pattern on the thoracic wall and afterwards on the limbs. Some loss of sensation was demonstrable in the skin over the lesions. No other signs were present (the state of the peripheral nerves is not recorded) and the chest X-ray was normal. Although no *Mycobacterium leprae* were seen, the histological diagnosis of "typical tuberculoid leprosy" was made. After a year's standard treatment, the nodular lesions had completely disappeared. The author suggests that leprosy bacilli must have been introduced at the time of the ritual scarifications through a breach in the skin.

He summarizes usefully the 9 recorded cases in which percutaneous introduction of leprosy bacilli is presumed, largely on anecdotal history.

[The present report leaves many crucial questions unanswered (and unasked). A very rare form of nodular tuberculoid leprosy, which disappeared spectacularly after a year's treatment, requires better substantiation than the author provides before it can be admitted as another instance of an inoculated leprosy infection.]

S. G. Browne

5. MYRVANG, B., NEGASSI, K., LØFGREN, M. & GODAL, T. Immune responsiveness to *Mycobacterium leprae* of healthy humans. *Acta Path. Microbiol. Scand. Sect. C*, 1975, v. 83, No. 1, 43-51.

"Immune responsiveness to *Mycobacterium leprae* was studied in various groups of healthy humans. Contacts of leprosy patients responded significantly more than non-contacts by the methods of leucocyte migration inhibition, lymphocyte transformation and early and late lepromin testing. By classifying responses of strengths found in non-contacts as negative, 71.2% of medical attendants, the main category of contacts, were responders by the leucocyte migration inhibition test, 44.2% by the lymphocyte transformation assay and 50.0% by the early lepromin reaction. On the other hand, no degree of the late lepromin reaction was found solely in *Myco. leprae*-exposed people. While the assays of leucocyte migration inhibition, lymphocyte transformation and early lepromin testing thus may be considered useful for detection of healthy individuals expose to *Myco. leprae*, the late lepromin reaction appears unsuitable as a measure of exposure. Besides the association of negative responses by leucocyte migration inhibition, lymphocyte transformation and early lepromin tests, there was in the group of non-contacts a significant quantitative correlation between early and late lepromin reactions. In the group of medical attendants significant correlations were observed between the results of all tests employed."

6. DASGUPTA, A., MEHRA, N. K., GHEI, S. K. & VAIDYA, M. C. Histocompatibility antigens (HL-A) in leprosy. *Tissue Antigens*, 1975, v. 5, No. 2, 85-7.

"HL-A antigens of 70 leprosy patients and 40 normal healthy individuals were determined by the standard microlymphocytotoxicity test. Both lepromatous and non-lepromatous leprosy patients were tested for the presence of 11 HL-A antigens, and the frequency of each specificity

was compared with that in a normal population of the same ethnic group. Although the statistical significance of HL-A8 specificity was found to be marginal in lepromatous leprosy patients, when using ordinary 2×2 statistics, there did seem to be a decreased frequency of HL-A9 among the non-lepromatous type. Other antigens tested did not reveal any significant differences between the two groups of subjects."

- 7 SHARMA, C. S. G. Effect of broxyquinoline and broxaldine in leprosy. *Lancet*, 1975, 15 Feb., 405.

A patient with lepromatous leprosy in a reaction stage was found to have intestinal amoebiasis and was advised to take a combination of broxyquinoline 500 mg and broxaldine 100 mg 3 times a day for 1 week, after which treatment for leprosy was to have been started. However, the patient did not return and was not seen again for 6 months, during which period he had continued to take broxyquinoline and broxaldine in the dosage suggested. He had not taken any specific treatment for leprosy, nor had he visited a leprosy centre. The lepromatous lesions showed "remarkable clinical improvement", and it was decided to try this treatment in further cases of lepromatous leprosy. So far 12 patients have been treated, 6 for 9 months and 6 for 6 months. Appreciable chemical and bacteriological improvement was noticed within 3-4 months, the nodules shrivelled and flattened, and there was a fall in both the morphological and bacteriological index [no details]. No serious adverse reaction was seen. The author, from Madras, suggests that the possibility that a combination of broxyquinoline and broxaldine might have some specific effect in leprosy should be investigated.

F. I. C. Apted

8. BERGEL, M. Actividad cancerigena de la diaminodifenilsulfona (D.D.S.). [Carcinogenic activity of diamino-diphenylsulphone (DDS).] *Publicões Cent. Estud. Leprol.*, 1973, v. 13, Nos 1/2, 30-40. English summary p. 41.

25 young rats were placed on a diet in which the content of diaminodiphenylsulphone was gradually raised to 0.3%. They were kept on this diet for 25 months, some being killed for examination at suitable intervals. In 11 rats examined within 15 months of the start, none showed tumours. Among 5 rats examined between 16 and 22 months, one rat showed highly malignant fibrosarcomas in the peritoneum and mesentery.

Eight rats were examined after 24 or 25 months and 7 of them showed tumours—reticularosarcomas, adenocarcinomas *etc.*, of the intestine, liver, spleen and thyroid. In 15 control rats on a normal diet, killed after 25 months, there were no significant tumours. The author refers to two reports that cancers are unduly common among leprosy patients treated with dapsone.

F. Hawking

9. BECHELLI, L. M. *et al.* BCG vaccination of children against leprosy: nine-year findings of the controlled WHO trial in Burma. *Bull. Wld Hlth Org.*, 1974, v. 51, No. 1, 93-9.

This further report on the findings of the WHO Burma trial will be read with great interest by all concerned with the control of leprosy. It should be studied in conjunction with the previously published reports of the trial and with the reports of the Uganda and Karimui trials [*Trop. Dis. Bull.*, 1971, v. 68, abstr. 83; 1974, v. 71, abstrs 739 and 740.]

A consistent protection rate of about 20% was observed during the second, third and fourth follow-up examinations. Previous infection with tuberculosis as indicated by tuberculin reactions of 10 mm or greater would not seem (on these results) to confer any substantial protection against subsequent challenge by leprosy.

The highest protection rate, that is 38%, was seen in children 0-4 years at intake.

No correlation could be found between the size of the tuberculin reaction and the form of leprosy developing in children, in either the group receiving BCG vaccination or in the control group. Most of these cases were of indeterminate or tuberculoid leprosy, and no case of

lepromatous leprosy appeared in either group during the study; the explanation advanced for this latter observation is that all detected persons with leprosy were treated.

The incidence of leprosy among household contacts was found to be 3.2 times that among others, irrespective of BCG vaccination.

The authors conclude that the protective effect of BCG vaccination found in the conditions of the Burma trial is not sufficiently substantial to warrant the widespread use of BCG with the aim of preventing leprosy or of affecting its trend in other areas in the world with similar epidemiological features.

The tables and the comment merit detailed and informed study.

S. G. Browne

10. IVANOVA, N. N. [The results of parallel investigation of the content of xanthurene and 5-oxiindolyacetic acids in the urine of patients with leprosy.] *Vest. Derm. Vener.*, 1975, No. 2, 16-19. [In Russian.]

The English summary appended to the paper is as follows:

"Parallel studies were carried out to determine the content of xanthurene acid (XA) according to the method of G. Ya. Vilenkina (1965) and of 5-oxiindolyacetic acid (OIA) by the method of Udenfriend *et al.* (1955) in the daily urine of 17 apparently normal subjects of the control group and of 57 patients with leprosy (42 [41?] with lepromatous, 12 undifferentiated, 3 with tuberculoid and 1 with dimorphic borderline forms). In 28 out of 42 patients with lepromatous leprosy the content of XA in the urine was found to be increased considerably (76.95 ± 7.68 mg/day, $P < 0.001$), as compared to that in the subjects of the control group (21.15 ± 1.96 mg/day). As the disease regressed the XA content showed a trend to normalization (46.16 ± 11). The XA content was increased also in 5 out of 12 patients with undifferentiated leprosy, in some patients with tuberculoid and borderline leprosy. Increased excretion of 5-OIA in the urine was observed in 21 out of 42 patients with lepromatous leprosy (4.27 ± 0.3 mg/day, $P < 0.001$ against 2.38 ± 0.189 mg/day in the controls), in 6 out of 12 patients with undifferentiated leprosy (5.13 ± 0.948 mg/day, $P < 0.011$) and in one patient with dimorphic leprosy (5.8 mg/day).

"The increase in the content of XA and 5-OIA acid in the urine of patients with leprosy attests to disorders of kinurenine and serotoninine ways of triptophane metabolism."

11. QUISMORIO, F. P., REA, T. H., LEVAN, N. E. & FRIOU, G. J. Immunoglobulin deposits in lepromatous leprosy skin. Presence of deposits in apparently uninvolved skin and occurrence of serum antiepithelial antibodies. *Arch. Derm.*, 1975, v. 111, No. 3, 331-4.

"Immunoglobulin deposits were detected in 10 of 13 biopsy specimens from apparently uninvolved skin of patients with lepromatous leprosy. There were deposits of IgM at the dermoepidermal junction in the skin of 5 patients, and deposits of IgM along the dermal collagen and elastic fibers in the skin of the other 5. The deposits were eluted with acid buffers and high molarity salt solution. Circulating IgC antibodies to intercellular substance of epithelial cells, similar to those present in pemphigus vulgaris, were found in 25% of patients with lepromatous leprosy who were studied. These antibodies appeared to be different from the skin-bound immunoglobulin deposits."

12. DELVILLE, J. Microbiologie de la lèpre. Comportement et affinités tinctoriales due bacille de Hansen dans les lésions lépreuses. [Microbiology of leprosy. Behaviour and staining properties of Hansen's bacillus in leprosy lesions.] *Ann. Soc. Belg. Méd. Trop.*, 1974, v. 54, No. 6, 457-62. English summary (6 lines).

This unorthodox and unconventional report will achieve the author's purpose if it causes microbiologists to question accepted standards for the identification, by its staining properties, of the causative organism of leprosy. After a brief summary of selected previous work, that has indicated that *Mycobacterium leprae* may possibly be present in all varieties of leprosy in forms

that are not revealed by standard staining procedures for acid- and alcohol-fast organisms, the author reports that the employment of variations of such techniques as those of Ziehl-Neelsen, Gram and Schiff, may reveal numerous bacilli that are not optically present when the ordinary Ziehl-Neelsen technique is used. Moreover, he has found many such bacilli in histological sections from lesions in which they are usually regarded as extremely scanty.

By Schiff staining, he concludes that these bacilli contain polysaccharides and, by an immunofluorescent technique using sera prepared from diphtheroidlike organisms, isolated by him from leprosy lesions, he deduces affinity, if not identity.

[These provocative suggestions need to be confirmed by other workers and the identity of the organisms established by available procedures (such as, for example, mouse footpad inoculation, the demonstration of specific phenoloxidases, and typical surface structure revealed by scanning electron microscopy) before their *bona fides* can be admitted.]

S. G. Browne

13. REES, R. J. W., McDOUGALL, A. C. & WEDDELL, A. G. M. The testis in mice infected with *Mycobacterium leprae*. *J. Path.*, 1975, v. 115, No. 2, 73-9.

"Following inoculation either locally or intravenously with *Myco. leprae* of human origin, the histopathology and bacteriology of the testis in experimental mice is described. Normal mice, and mice rendered immunologically deficient by thymectomy and whole-body irradiation, were studied.

"Attention is drawn to a heavy bacillation of the testis in mice from both groups. Bacilli were found in and beneath albuginea, but mainly in interstitial cells and in macrophages surrounding the tubules. The percentage of solidly staining bacilli was high, and globi were frequent.

"The study showed that the testis in mice is particularly favourable for the lodgment and multiplication of *Myco. leprae* following either local or intravenous inoculation.

"The significance of this in relation to the metabolism of the leprosy bacillus and to the frequent occurrence of testicular damage in the lepromatous male patient is discussed."~

14. MILLAN, J. & LE CORROLLER, Y. Le dépistage systématique dans la lutte contre la maladie de Hansen: résultats obtenus en Guadeloupe dans le secteur de Grande-Terre. [Systematic case-finding in the leprosy campaign. Results obtained in Guadeloupe, in the Grande-Terre sector.] *Méd. Afr. Noire*, 1974, v. 21, No. 10, 695-703.

The authors summarize the results obtained through an intensive case-finding programme in a sector containing about half of the total leprosy patients in a country of a third of a million inhabitants and a leprosy prevalence rate of 5.7 per 1000.

As regular whole-population surveys are impracticable, the programme depends upon the application of widely-accepted principles to ensure that leprosy is diagnosed as early as possible. General practitioners discover, in their ordinary clinics, about half the total number of leprosy patients diagnosed annually. Co-operation with other doctors who regularly examine selected populations (for example, work-people) is another fruitful source of new cases. The examination of contacts should, it is admitted, be more extensive and better organized than it is. The most hopeful feature of the programme was the introduction of a mobile team, which concentrated on the examination of schoolchildren; 52% of new cases were discovered through this activity, and these included 46% of the new cases of lepromatous leprosy. With the lowering of the average age at diagnosis, the numbers of schoolchildren suffering from self-healing forms of leprosy have increased, but the authors consider that the efforts are justified if some patients with early lepromatous or near-lepromatous leprosy are thereby brought to light.

S. G. Browne

15. KRONVALL, G., HUSBY, G., SAMUEL, D., BJUNE, G. & WHEATE, H. Amyloid-related serum component (protein ASC) in leprosy patients. *Infection & Immunity*, 1975, v. 11, No. 5, 969-972.

"The presence of amyloid-related serum component, protein ASC, in serum samples from 63 leprosy patients was investigated. Protein ASC was detected in 38% of the patients. A correlation to the disease spectrum of leprosy was apparent: polar lepromatous cases, 64% positive; borderline lepromatous, 50%; borderline tuberculoid, 36%; subpolar tuberculoid, 17%; and polar tuberculoid, negative. Antibody activity against the antigen of *Mycobacterium leprae* was also determined, showing a similar correlation to the disease spectrum. Serum samples from 23 apparently healthy Ethiopians serving as controls showed a protein ASC incidence of 22%. This figure is significantly higher than the frequency found by others among healthy Norwegian blood donors. Immunoglobulin M levels among patients were elevated in the borderline lepromatous and polar lepromatous groups. The three tuberculoid groups did not differ in this respect from the control group but were all elevated as compared to a normal Caucasian serum pool. Although raised immunoglobulin M levels seemed to parallel increased frequencies of protein ASC in the patient groups as well as in controls, this correlation might be only secondary to a primary derangement in T-cell function."

16. LIM, S. D., TOURAINE, J. L., STORKAN, M. A., CHOI, Y. S. & GOOD, R. A. Leprosy XI. Evaluation of thymus-derived lymphocytes by an antihuman T-lymphocyte antiserum. *Int. J. Lepr.*, 1974, v. 42, No. 3, 260-265.

"T lymphocytes were evaluated in the peripheral blood of patients with various forms of leprosy, using a heterologous antiserum specific for human T cells. A significant decrease in T lymphocyte numbers was observed in cases of active lepromatous leprosy but not in the active lepromatous, borderline or indeterminate forms of the disease.

"Patients with lepromatous leprosy resistant to chemotherapy showed a lower level of T lymphocytes than did drug sensitive patients, while patients with lepromatous leprosy complicated by *erythema nodosum leprosum* showed higher levels than did those with uncomplicated lepromatous leprosy. Evaluation of T lymphocytes by microcytotoxicity test with the anti T-cell serum used in this study proved to be as accurate as the nonimmune or spontaneous formation of rosettes with the sheep red blood cells after incubation at 37°C."

17. KAUR, S., CHAKRAVARTI, R. N. & WAHI, P. L. Liver pathology in leprosy. *Lepr. India*, 1974, v. 46, No. 4, 222-225.

"Twenty six patients suffering from leprosy, classified clinically, bacteriologically and histopathologically as lepromatous-14, tuberculoid-9 and dimorphous-3, have been studied for liver involvement.

"Thirteen out of fourteen lepromatous patients showed specific granulomata in the liver. Acid fast bacilli were found in 12. A direct relationship between the intensity of skin lesions and hepatic involvement was found. Five out of the nine tuberculoid cases showed epithelioid granulomata. Acid fast bacilli were not found in any of these. Two of the dimorphous cases showed granulomata and one was positive for acid fast bacilli. Amyloid deposit was not found in any of the liver biopsies."

18. GUPTA, J. C., GUPTA, D. K. & GUPTA, A. K. Hepatic lesions in leprosy. *Lepr. India*, 1974, v. 46, No. 4, 226-233.

"Liver biopsies from 50 cases of leprosy, 43 cases of lepromatous leprosy and 7 cases of nonlepromatous leprosy, admitted into the skin, V.D. and Leprosy department of the Medical College Hospital, Jabalpur, during the period from April 1971 to October 1972 have been studied histopathologically in detail employing H & E stain as well as special staining techniques for reticulin, amyloid and A.F.B.

"Granuloma constituted the commonest specific lesion in liver in both the major types of

leprosy in lepromatous and nonlepromatous. Other changes noted included, Kupffer's cell hyperplasia, reticulin condensation in and around granuloma, increased connective tissue and cloudy swelling. No amyloid deposit could be detected. A.F.B. could be demonstrated in granulomas in all the cases of lepromatous leprosy.

"The changes noted have been discussed and compared with those of the previous workers.

"It is postulated that granuloma constitutes the commonest and specific type of lesion in liver in cases of leprosy of the two major types. Other changes noted could be attributed to long duration of illness or simultaneous malnutrition or associated other infections or effects of prolonged administration of drugs."

19. KELKAR, S. S., NIPHADKAR, K. B., KHARE, P. M. & GHARPURAY, M. B. **Environment and carriage of hepatitis B antigen in leprosy.** *Indian J. Med. Res.*, 1974, v. 62, No. 12, 1794-1799.

"Hepatitis B antigen carriage was studied in 152 patients with leprosy attending the out-door of the Sassoon General Hospitals, Poona. This group consisted of 37 cases of lepromatous leprosy and 115 of tuberculoid leprosy. Sera from the patients were studied for presence of hepatitis B antigen by both immunoelectroosmophoresis and agar-gel diffusion. Agar-gel diffusion was much less sensitive than immunoelectroosmophoresis. The carriage rates for hepatitis B antigen were 13.5% in the lepromatous leprosy patients (5 positive in 37) and 4.3% in the tuberculoid leprosy patients (5 positive in 115). The accommodation, sanitation and source of water of each patient was established by careful interrogation. The environment, in terms of these three parameters was best with tuberculoid leprosy patients, less so in the lepromatous leprosy patients not carrying the hepatitis B antigen and worst in the 5 patients with lepromatous leprosy and carrying the hepatitis B antigen. Carriage of hepatitis B antigen appears to be related to poor environmental circumstances which seem to favour transmission of the hepatitis B virus.

20. LEVY, L. **Superinfection in mice previously infected with *Mycobacterium leprae*.** *Infection & Immunity*, 1975, v. 11, No. 5, 1094-1099.

"Previous studies of the protection of mice by prior infection with *Mycobacterium leprae* in one hind footpad against challenge with *Myco. leprae* in the opposite hind footpad had produced conflicting results; therefore, the problem was restudied. In several experiments, BALB/c mice were inoculated first in the right hind footpad with 5000 *Myco. leprae* and then challenged in the left hind footpad with 5000 *Myco. leprae* of the same strain at intervals after primary infection, at the same time that uninfected mice were inoculated. Multiplication of the *Myco. leprae* of the secondary challenge inoculum occurred at the same rate and to the same level as multiplication in uninfected mice when challenges were made soon after primary infection. Multiplication was slowed but proceeded to the same level in previously infected as in uninfected mice when the challenges were administered between 76 and 106 days after primary infection (47 to 17 days before the *Myco. leprae* of the primary inoculum had multiplied to the level of 10^6 organisms per footpad). Finally, the *Myco. leprae* of a secondary challenge administered at the time that the organisms of the primary inoculum had multiplied to 10^6 per footpad or later not only multiplied more slowly in previously infected than in control animals, but multiplication in the previously infected animals reached a lower maximum. These results are similar to those observed when mice previously infected with *Myco. bovis* (BCG), *Myco. marinum*, *Toxoplasma gondii*, or *Besnoitia jellisoni* were challenged with *Myco. leprae*."

21. JOB, C. K., CHACKO, C. J. G., VERGHESE, R. & PADAM SINGH, S. **Enhanced growth of *Myco. leprae* in the foot pads of thymectomized irradiated mice.** *Lepr. India*, 1974, v. 46, No. 4, 216-221.

"In 10 separate experiments 10 different strains of 10^4 *Myco. leprae* obtained from untreated lepromatous leprosy patients were injected into the foot pads of thymectomized irradiated (T 900r) Swiss albino mice. Normal mice were also given the same number of organisms into

their foot pads and were used as controls. It was shown that in all the 10 experiments immunological suppression by thymectomy and total body irradiation produced a marked enhancement of the growth of *Myc. leprae* in the foot pads which is 10 to 100 times more than that in normal mice. Controlled environmental temperature of the animal house at 20-22°C and careful screening of the T 900r mice from exposure to other infections were necessary for these animals to survive for long periods. In normal mice the infection with *Myc. leprae* persisted for its life time without producing any ill effects on them."

22. LEVY, L., NG, H., EVANS, M. J. & KRAHENBUHL, J. L. **Susceptibility of thymectomized and irradiated mice to challenge with several organisms and the effect of dapson on infection with *Mycobacterium leprae*.** *Infection & Immunity*, 1975, v. 11, No. 5, 1122-1132.

The authors conclude that because these thymectomized and irradiated mice "were not greatly immunosuppressed, they would not have provided a model of human lepromatous leprosy suitable for chemotherapeutic studies".

23. HOLMES, I. B. **Minimum inhibitory and bactericidal dosages of rifampicin against *Mycobacterium leprae* in the mouse foot pad: relationship to serum rifampicin concentrations.** *Int. J. Lepr.*, 1974, v. 42, No. 3, 289-296.

"The minimum dietary dosage of rifampicin (RMP) suppressing the growth of eight strains of *Mycobacterium leprae* in the mouse foot pad has been determined. Graded dosages of the drug were administered continuously to mice infected with *Myc. leprae* from the day of inoculation. The growth of six strains was suppressed by 0.001% RMP in the diet: the remaining two strains were suppressed by 0.0003% and 0.003% RMP respectively.

"By use of the kinetic technic of Shepard, the bactericidal effect on three strains of *Myc. leprae* of graded dietary dosage of RMP administered for 56 days has been determined. Considerable bactericidal activity was observed with dosages greater than the minimum inhibitory dosage (MID). The MID (0.001%) was bactericidal against strain SBL 16237 (1.17% survival), bacteriostatic against strain SBL 16325 (100% survival) and weakly bactericidal against strain SBL 16263 (13.9% survival).

"Serum RMP concentrations in mice receiving graded dietary dosages of the drug were estimated by a microbiological assay technic using *Sarcina lutea*. A linear relationship between dosage and resultant serum RMP concentrations was found. The MID of RMP for six *Myc. leprae* strains (0.001%) was equivalent to a serum RMP concentration of 0.2 µg/ml. For the two remaining strains the MID was equivalent to a serum concentration of 0.06-0.09 and 0.9 µg/ml respectively. The minimum bactericidal dosage of RMP (0.003%) gave serum levels of approximately 0.9 µg/ml. Serum RMP concentrations equivalent to the minimum inhibitory and bactericidal dosages for *Myc. leprae* are maintained for long periods in patients receiving a daily RMP dosage of 600 mg which has been used in recent clinical trials of the drug in the treatment of leprosy."

24. LEVY, L. **The activity of chaulmoogra acids against *Mycobacterium leprae*.** *Am. Rev. Resp. Dis.*, 1975, v. 111, No. 5, 703-705.

"The activity of the crude sodium salts of the fatty acids of chaulmoogra oil and of hydnocarpic and chaulmoogric acids against *Mycobacterium leprae* was studied in mouse footpad infection. Multiplication of the organisms was inhibited when the salts were administered intraperitoneally and subcutaneously 3 times per week, and when chaulmoogric acid was administered intraperitoneally 5 times per week in half the equivalent dose. Dihydrochaulmoogric acid was also active, whereas palmitic acid was not. Hydnocarpic acid administered intraperitoneally once per week in a dose equivalent to half that of the sodium salts of the chaulmoogra fatty acids was not effective. The demonstration that chaulmoogra fatty acids possess activity against *Myc. leprae* lends weight to our earlier suggestion that a

study of compounds analogous to these acids may yield effective antimicrobial agents with a unique mechanism of action."

25. LEVY, L. & ULLMANN, N. M. Inhibition of multiplication of *Mycobacterium leprae* by several antithyroid drugs. *Am. Rev. Resp. Dis.*, 1975, v. 111, No. 5, 651-655.

"Multiplication of *Mycobacterium leprae* in the mouse footpad was inhibited when mice were fed, mixed in their diet, 0.05% methimazole, 0.066% USP thyroid powder, methimazole plus thyroid powder, 0.15% 5-n-heptyl-2-thioxo-4-thiazolidinone, 0.1% propylthiouracil, and 0.1% thiambutosine for 154 days, beginning on the day of inoculation. All of the treatment regimens, except for the 2 containing thyroid powder, decreased the plasma concentrations of thyroxine and protein-bound iodine. It is suggested that the 2 antithyroid drugs, methimazole and propylthiouracil, and the 2 antimicrobial agents, heptylthioxothiazolidinone and thiambutosine, all of which possess structural features in common, may exert the antithyroid and antimicrobial effects through a common mechanism."

26. YOSHIZUMI, M. O., KIRCHHEIMER, W. F. & ASBURY, A. K. A light and electron microscopic study of peripheral nerves in an armadillo with disseminated leprosy. *Int. J. Lepr.*, 1974, v. 42, No. 3, 251-259.

"The lesion of peripheral nerve observed in an armadillo which developed lepromatoid leprosy following experimental infection with *Myco. leprae* was found to be similar by light and electron microscope examination to the peripheral nerve lesion of human lepromatous leprosy. Bacilli were found primarily within macrophages, endothelial cells, perineurial cells and Schwann cells of unmyelinated fibers. Destruction of nerve tissue appeared to have a perivascular distribution. The pattern of bacillation with predominant involvement of blood vessels suggests hematogenous dissemination of *Myco. leprae* in the armadillo. These observations taken together constitute evidence that armadillos with the disseminated form of leprosy are suitable models for the study of the neural lesions of human lepromatous leprosy.

27. MATSUO, Y. Studies of *Mycobacterium lepraemurium* in cell culture. I. Continuous multiplication in cultures of mouse foot pad cells. *Jap. J. Microbiol.*, 1974, v. 18, No. 4, 307-312.

"A serial increase in the number of *Mycobacterium lepraemurium* with successful subcultures has been obtained in the mouse foot pad (MFP) cell culture. Special attention has been given to maintaining the infected cells for longer periods: (1) the infected cells were incubated at 30°C rather than at 37°C, and (2) the concentration of serum in the culture medium was reduced from 10 to 2% as soon as a monolayer growth of the transferred cells was obtained. There have been cumulative bacterial increases of 1.47×10^{17} and 1.84×10^{15} fold for the Kurume-42 strain during a period of 1255 days, and 2.23×10^9 and 3.89×10^5 fold for the Hawaiian strain during periods of 831 and 572 days. The overall generation times were estimated at 22.0, 24.8, 26.8, and 30.8 days, respectively. All attempts to grow the acid-fast bacilli obtained in cell cultures on artificial culture media have failed. The ability of the organisms to produce typical lesions in mice has been well preserved."