Lepr. Rev. (1979) **50,** 162–179

Abstracts

25. WHITE, S. J., STONE, M. M. & HOWLAND, C. **Genetic factors in leprosy: a study of children in Uganda.** *J. Hyg., Camb.,* 1978, 80, 205–215.

The clustering of leprosy within families has led to considerable discussion in the literature, with some authors interpreting it as a reflection of hereditary—i.e. genetically determined—susceptibility, and others claiming that it reflects only the intimate contact of family members within the home. There is now much evidence that each of these factors (genetic and contact) plays a role in determining the distribution of leprosy within communities. On the other hand, most published studies have concentrated on only one of the factors in interpreting data on the distribution of leprosy; and, in so doing, many authors have overlooked the difficult problem posed by the fact that the two are closely confounded. As people generally have closest contact with their closest relatives, a risk associated with one factor will be apparently associated with the other as well. This study by White *et al.* is noteworthy in its effort to measure both factors simultaneously, in an attempt to assess the relative importance of each.

The data base consists of information on leprosy prevalence at the onset of, and leprosy incidence during the (8 years) course of, the MRC trial of BCG against leprosy, which was begun in Uganda in 1960. The total population at risk consisted of 20,990 children who were related to, or who had been in contact with, a known case of leprosy. Familial relationships between "at risk" children and nearest leprosy cases were expressed in terms of degree of consanguinity: fathers, mothers and full siblings = 1; half siblings of children and full siblings of their parents = 2; etc. (One flaw of the study is the author's insistence on these as "exact genetic relationship" data—a supposition which appears mildly over-optimistic in the light of well-recognized problems in the collection of such data and the absence of their objective verification in this study.) Contact relationships between "at risk" children and nearest leprosy cases were described in four categories: i.e. "house", "compound", "visiting" or "none". All children could then be broken down into subgroups in terms of their genetic and their contact relationships with the nearest known leprosy patient of lepromatous or non-lepromatous type. Analysis of these data consisted of calculating prevalence rates and incidence rates of leprosy within each subgroup, standardizing for age, tuberculin or vaccination status, and for proportion of multiple or lepromatous contacts. It was hoped that these rates would allow separation of the effects of genetic and of contact relationships between source cases and "at risk" groups. The methodology and standardizing procedures are elegant, and should serve as a model for future studies of the epidemiology of leprosy.

The results are well presented and interesting, even though negative. It proved difficult to separate out close genetic from close contact relationships, as these factors were so highly confounded (approximately 90% of first-degree relative contacts were in the home). Considering the data as a whole, however, there was little evidence for a gradient of risk associated with genetic relationship, and this was virtually totally removed when contact was taken into account. The authors recognize that their data do not refute the evidence for some role for genetic determination in leprosy susceptibility; but they are perhaps correct in their conclusion that, despite several shortcomings in this study due to the fact that it was not originally designed as a genetical investigation, it "should have been sufficient to reveal any important genetic influence." One may agree with the authors, therefore, that once an allowance has been made for extent of physical contact, the degree of consanguinity between known cases and apparent susceptibles does not appear to have been a major factor determining the distribution of clinical leprosy in this Uganda population.

P. E. M. Fine

26. AMBROSE, E. J., KHANOLKAR, S. R. & CHULAWALLA, R. G. **A rapid test for bacillary resistance to dapsone.** *Lepr. India,* 1978, v. 50, No. 2, 131–143.

To date, the only laboratory test of drug resistance in *Mycobacterium leprae* is based on the multiplication of leprosy bacilli in the footpads of mice fed with appropriate concentrations of drug in their diet. Such testing takes from 5.5 to 12 months to complete. Therefore a more rapid, and preferably *in vitro,* test is urgently needed, especially as clinical proof of resistance may take anything from 3 months to 5 or more years, requires close supervision of the patient, and may not be practicable in many cases.

Unfortunately, although a number of workers have claimed to have grown *M. leprae in vitro,* the consensus of opinion is that to date no claim has been fully and independently substantiated. Therefore Ambrose and his colleagues decided on a new approach, namely, to maintain leprosy bacilli obtained freshly from the patient in what they considered to be the best medium at present available, for the shortest possible period necessary to assess their rate of metabolism and growth potential, at a stage "prior to the likely emergence of contaminating Mycobacteria . . ."

The medium chosen was that of Murohashi and Yoshida (1975), a simple synthetic medium containing yeast extract. Great care was taken to maintain sterility while obtaining the skin biopsy specimens and extracting the leprosy bacilli. The latter was achieved by a simple two-stage technique; which involved placing the minced tissue in ice-cold distilled water to lyse all the human cell membranes so releasing the intracellular bacilli, and at the same time eliminating host cells. The initial inoculum size was 10^7 bacilli, but with increasing experience (and skill) this was reduced to 10^6 bacilli (containing perhaps 50,000 viable *M. leprae*) thereby enabling 50–100 cultures to be set up from each biopsy.

A radioactive assay was developed, using labelled [^{3}H]thymidine and [^{3}H]DOPA, and read by scintillation counter at 0, 6 and 9 days. Tubes assayed included standard cultures, heat treated samples, and cultures containing various concentrations of dapsone or rifampicin, and in one experiment clofazimine was also studied. It is claimed that good reproducibility could be achieved in the counts from similar tubes. Results obtained with [^{3}H]thymidine correlated well with those using [^{3}H]DOPA. Good correlation was also obtained between the *in vitro* tests now repeated and drug sensitivity tests performed on two patients in mice.

The work recalls the earlier studies of Hart and Valentine (1960) on the growth (but not multiplication) of *M. lepraemurium in vitro.* It is an exciting development, and further reports are awaited with interest. The advantages of obtaining the results of drug sensitivity tests within about 2 weeks are obvious. The method could be adopted for the rapid screening of new drugs against *M. leprae* and already is being applied to the rate of kill *in vivo* of *M. leprae* in lepromatous patients receiving different drug regimens in controlled clinical trials. Confirmation of the method from other centres is eagerly awaited. At the same time it must be remembered that the technique requires considerable expertise, as well as access to radioisotopes and to scintillation counting; and therefore could only be carried out in main universities and research centres possessing such facilities.

Murohashi, T. and Yoshida, K. (1975). *Acta Leprolog.* **58,** 5. Hart, P. D'A. and Valentine, R. C. (1960). *Nature* **185,** 58.

M.F.R. Waters

27. US LEPROSY PANEL (US–Japan Cooperative Medical Science Program) AND THE LEONARD WOOD MEMORIAL. **A statistical analysis of two chemotherapy trials in lepromatous leprosy: I. The response to therapy as measured by inoculation of mice. II. Interactions among patient variables.** *Am. J. trop. Med. Hyg.,* 1978, v. 27, 1005–1014 and 1015–1018.

I. The first paper is concerned with the correlation between certain pretreatment variables and the subsequent rate at which bacilli in skin biopsies were rendered non-infective to mice. The treatment regimen was found to be the most important determinant of the rate of loss of infectivity. In addition, the LAFB (log of the bacterial count in a suspension prepared for inoculation) and the LIB (logarithmic index of biopsies) were found to affect significantly the response to treatment in the early part of the trial, though not after a period of 24 weeks when the effect of the drugs was paramount. The influence of bacterial numbers was most evident when there was

no big difference in the efficacy of the drug regimens to be compared. The possibility that this apparent effect of numerous bacilli might in reality be due to an inhibitory effect of tissue has not yet been excluded. Of the pretreatment variables tested, age had some significance in trial I, clinical and histological classification (BL or LL) in trial II. This influence was noted after periods of 16 and 12 weeks treatment respectively. Age and classification were not related to the pretreatment values of the LIB or LAFB. Stratification of patients by bacterial counts in skin lesions is recommended for future short-term drug trials in lepromatous leprosy.

The conclusion that bacterial numbers in pretreatment biopsies have a bearing on the subsequent rate of killing of bacilli during a drug trial, if confirmed, is obviously important. Killing of bacilli is the measurement of greatest importance in assessing drug activity. By contrast, classification is more closely related to lysis of bacilli and the fall in bacterial numbers, which is a function of immunity. However, there is no explanation of why a high bacterial count should be associated with an apparent delay in reaching non-infectivity. If it is not due to a dilution effect on a tissue inhibitor of multiplication in the mouse, as the authors suggest, one can think only that a large lesion may contain more "persister" bacilli. This much seems to be clear though the regression analysis, as given, is not comprehensible to a non-mathematician.

II. The second paper deals with the inter-relationships between various characteristics analysed at the commencement of the trial. The subsequent progress of the patient and the loss of infectivity are not under consideration. Sex was found to be associated with the age of the patient and his histological classification; disproportionately large numbers of older patients and of BL patients were male. Classification by clinical and histopathological criteria were closely associated, but many patients classified BL histologically were found to be LL clinically (the details given in the text are by no means clear on this point). Similarly, the bacterial indices (LAFB, LIB and BI) were found to be correlated with each other, though not perfectly. Evidence is given for thinking the LAFB to be the most precise representation of numbers, which it should be as it is a direct count. (In one place BI is misprinted as LIB.)

No correlation was found between classification and bacterial indices. This may have been largely due to the requirement that biopsies should contain enough bacilli to make inoculation of mice practicable; thus, small BL lesions with low counts would have been excluded. (It must be allowed that there is considerable overlap between groups as regards bacterial indices; see *Bull. Wld Hlth Org.*, 1974, v. 51, 451.)

D. S. Ridley

28. SHEPARD, C. C., WALKER, L. L. & VAN LANDINGHAM, R. **Heat stability of *Mycobacterium leprae* immunogenicity.** *Infect. Immun.*, Oct. 1978, v. 22, No. 1, 87–93.

The authors have extended their previous observation that the proliferation in mice of a small challenge dose of *M. leprae* (5000 organisms) can be inhibited by "vaccination" with 10^7 *M. leprae*, or 10^7 BCG one month before challenge.

Thus when normal CFW mice are challenged in the footpad with 5×10^3 *M. leprae* bacilli from human, mouse, or armadillo tissues, there is slow multiplication up to a plateau level of about 10^6 organisms after 6 months. The authors monitored this growth curve and killed the vaccinated mice when the controls reached the plateau, and also 90 days later. The organisms in the challenged footpads were counted. In addition, the size of the lymph-node draining the vaccination site was measured at intervals.

The vaccines used with or without the pretreatments described below were 10^7 BCG, grown in a Tween-albumin medium, or 10^7 *M. leprae* from armadillo livers. For most experiments the *M. leprae* was purified by centrifugation, and gentle trypsinisation, but organisms further purified by the two-phase polyethylene glycol/dextran system gave similar results. Vaccines were usually injected intradermally into the right flank, 28 days before challenge, although in one experiment vaccination into a footpad proved equally effective.

The main studied variable in this paper was the effect on protective efficacy of killing the "vaccines". This was done by heating to 60°C, 80°C or 100°C for 30 min; by freeze-thawing; by autoclaving at 15 lb/sq. in. for 15 min, or by incubation in 2% phenol for 16 h at 37°C. It was consistently shown that whereas killing the BCG greatly reduced its efficacy, killed *M. leprae* protected as well as live organisms. Varying the technique used to kill the organisms, or the medium in which they were suspended resulted in small, not always reproducible differences,

attributable in part to aggregation of the organisms, and consequently enhanced retention at the vaccination site.

The degree of enlargement of the lymph-node draining the vaccination site usually correlated with the degree of protection.

In conclusion the authors argue that the mechanism of protection is likely to be a specific cell-mediated immune response to the challenge dose, and imply that since *M. leprae* can be used after autoclaving, their findings point to the possibility of a killed vaccine, safe for use in man.

However, this mouse model must be interpreted with caution. There is at present no evidence that protection in this system is due to T-lymphocyte-mediated recognition of the 5000 bacilli used for challenge. Protection is seen only when the vaccine induces persistent enlargement of the draining lymph-node. This is *not* an expected prerequisite for the generation of a straight forward *M. leprae*-recognizing T-cell population, and strongly implies that protection is largely due to the maintenance of a state of macrophage activation by a continuing response to the vaccine itself. Against this interpretation is an observation which may imply that non-specifically activated macrophages occur *only* at the vaccination site. Thus Patel and Lefford (1978, *Infect. Immun.,* v. 20, 692–697) have reported that following vaccination with killed *M. leprae,* activated macrophages capable of nonspecifically destroying *Listeria monocytogenes* were present at the vaccination site itself but were not demonstrable following intravenous challenge. Nevertheless, the absence of a nonspecific mechanism capable of killing intravenous *Listeria* does not eliminate the possibility that there is one capable of killing subcutaneous *M. leprae.*

Even if *M. leprae*-recognizing T-cells are evoked by the vaccine, it is doubtful whether their presence can be demonstrated by the protocol used. This doubt is derived from certain bizarre features of leprosy infection in the mouse. Thus when other mycobacteria such as *M. lepraemurium* or *M. avium* are injected into normal mice, the larger the challenge dose, the greater is the likelihood of proliferation and dissemination of organisms. With *M. leprae,* the reverse is true. Larger doses, such as 10^6 or 10^7 bacilli, fail to proliferate, and merely immunize the animal, whereas if only 5000 organisms are injected, they will multiply to a plateau of about 10^6 bacilli. Only in the absence of T-lymphocytes will proliferation continue beyond this point. We can conclude that once a sufficient load of *M. leprae* is present, mouse T-cells are perfectly capable of mounting an effective response, without vaccination. Moreover, *M. leprae* proliferates slowly, but evokes a response within a few days so that in a mouse challenged with an *immunogenic* number of bacilli, any accelerated response due to vaccination would be indistinguishable from the response in unvaccinated controls.

The authors avoid this rapidly evoked and effective response by challenging the mice with a subimmunogenic dose of only 5000 bacilli. The available suspensions of *M. leprae* contain notoriously little soluble antigen, of which there can be only about 10 pg in 5×10^3 organisms. The actual quantity of any one specificity released at any one time by 5000 very slowly proliferating organisms may well be below the threshold for effective T-cell recognition, even by a primed population. Thus the use of this tiny challenge dose may bias the system in favour of the non-specific macrophage activation mechanism, which will accompany the persistent reaction to vaccine, occurring in the enlarged draining node.

This is an important objection, but it can be resolved. It will be necessary to prove that T-lymphocytes recognizing *M. leprae* are generated (even by BCG) and that such T-cells will protect when transferred into normal mice, in which macrophage activation is not a problem. It should also be possible to demonstrate effective vaccination using an organism which *does* cause the development of T-lymphocytes capable of recognizing the antigens of the leprosy bacillus, but which does *not* itself cause chronic lymph-node enlargement and macrophage activation. It is at present puzzling that organisms known to have these properties have failed to protect in Dr Shepard's system (Shepard, Walker, and Van Landingham (1978), *Infect. Immun.,* v. 19, 341–394).

The other main point, made in this paper, is the immunogenicity of killed *M. leprae,* which has been confirmed in several other laboratories. This finding has surprised many workers, because the current dogma states that killed mycobacteria are not immunogenic. This dogma has arisen in spite of the fact that killed *M. tuberculosis* has been known to be fully immunogenic in the guinea-pig since the observations of Petroff in the 1920's. It is now clear that most species of mycobacteria are immunogenic when killed, and evoke vigorous T-lymphocyte responses. In this respect they resemble *Corynebacterium parvum,* which is routinely used killed. The erroneous dogma arose because certain members of the slow-growing subgenus, in particular

some (but not all) strains of the *M. avium/M. lepraemurium* group, and of the BCG/*M. tuberculosis* group, and *M. kansasii*, are indeed poorly immunogenic in the mouse, when killed. Usually organisms are pathogenic for those strains of mice in which they lack immunogenicity when killed. Perhaps a hint of the same phenomenon is seen with *M. leprae* in man. Thus *M. leprae* may be pathogenic only in those individuals who respond poorly to killed organisms, and in whom the Mitsuda lepromin reaction is consequently negative. This would suggest that a killed *M. leprae* vaccine will fail in those who need it most, just as killed *M. tuberculosis* or killed *M. kansasii* fail to protect susceptible mice from tuberculosis, or *M. kansasii* infection.

In summary, the fascinating and painstaking data contained in this paper appear superficially simpler to interpret, but are really at the heart of one of the most obscure corners of mycobacterial immunology.

G. A. W. Rook

The abstracts which follow are reprinted from the Tropical Diseases Bulletin, *September–December, 1978, and January, 1979, through the courtesy of the Director, Bureau of Hygiene and Tropical Diseases, London. They are classified according to subject.*

1. MICROBIOLOGY

29. SREEVATSA, SENGUPTA, U., RAMU, G. & DESIKAN, K. V. **Evaluation of bacteraemia in leprosy patients.** *Lepr. India,* 1978, v. 50, No. 3, 381–387.

"Thirty-five patients with leprosy have been screened for bacteraemia by haemolysis (HL), leucocyte adherence (LA) and buffy coat (BC) methods and the results have been compared. The HL method has yielded not only higher number of acid-fast bacilli (AFB) but also has detected more frequently AFB in blood of leprosy patients as compared to other methods. Further, it has been established that the skin over the cubital fossa does not play any significant role in contaminating blood samples while sampling blood by venepuncture."

30. HIRATA, T. **Electron microscopic observations of cell division in *Mycobacterium leprae* by means of serial ultrathin sectioning.** *Int. J. Lepr.,* 1978, v. 46, No. 2, 160–166.

"The division of *Mycobacterium leprae* in skin was studied in the ultrathin sections at the electron microscopic level. A few dividing bacilli were observed. The division seemed to be accomplished by inward extension of both the cell wall and the cytoplasmic membrane into the cytoplasm of the bacillary cell to form a septum. The intracellular membranous organelle (mesosome) is assumed to play a role in division."

31. KIRCHHEIMER, W. F. & SANCHEZ, R. M. **Examination of North American armadillos for mycobacteriosis.** *Lepr. India,* 1978, v. 50, No. 2, 156–160.

"Between 1 January 1974 and 31 December 1977, Carville has found no leprosy-like mycobacteriosis in 373 armadillos. Two hundred and eighty-two of these armadillos were caught in Louisiana, 78 in Florida and 13 in Texas.

"Seventy-five of the Louisiana armadillos were caught by personnel from the Louisiana Wildlife and Fisheries Commission in the area where Walsh *et al.* said they found 10 per cent 'naturally' infected armadillos.

"Two hundred and seven of Carville's armadillos came from the most human-leprosy prevalent part of Louisiana.

"Alleged claim of man to armadillo transmission of leprosy as an explanation for existence of leprous armadillos in nature also is at odds with South American findings and conditions.

"Independent verification of the claim of Walsh *et al.* is called for and if confirmed investigation of the various possible ways such a situation might have arisen."

[See *Trop. Dis. Bull.,* 1976, v. 73, abstr. 896; 1977, v. 74, abstr. 2803.]

32. NAKAMURA, M., CHIBA, K. & TANAKA, Y. **[Multiplication of** *Mycobacterium lepraemurium* **in cell-free liquid and medium. 12. Growth of** *Myco. lepraemurium* **grown on egg-yolk solid medium in the liquid medium.]** [NAKAMURA, CHIBA & TANAKA.] *Jap. J. Lepr.,* 1977, v. 46, No. 3, 92–97. **[13. Growth evaluation; sediment smear method (SSM).]** [NAKAMURA.] *Ibid.,* 98–103. **[14. Initial growth curve of** *Myco. lepraemurium* **in cell-free medium.]** [NAKAMURA & CHIBA.] *Ibid.,* 104–107. [**15. Growth stimulating effects of adenosine and thymidine on** *Myco. lepraemurium in vitro.*] [NAKAMURA.] *Ibid.,* 108–111. [In Japanese.] English summaries.

[For earlier parts see *Trop. Dis. Bull.,* 1978, v. 75, abstr. 514.]

33. MORI, T. **Study of a growth factor for** *Mycobacterium lepraemurium.* **I. Minimal medium.** *Int. J. Lepr.,* 1978, v. 46, No. 2, 125–132.

"A growth promoting factor is contained in the petroleum ether or acetone extracted residue of lyophilized dry egg yolk. Egg white, horse serum, soybean powder, bovine serum albumin, egg albumin and milk were used in *M. lepraemurium* culture attempts as protein sources instead of yolk lipoprotein. None of these substances promoted the growth of *M. lepraemurium.*

"One percent egg white medium was prepared from the mixture of one part 1% Ogawa basal medium to two parts egg white, adjusted to pH 6.1. This medium does not permit the growth of *M. lepraemurium* but permits bacillary survival for two months. This medium is most suitable as a minimal medium to investigate growth factors of *M. lepraemurium.* Utilizing the minimal medium, the following substances were tested for growth promoting activity: lecithin, cholesterol, petroleum ether extracted fraction of yolk, butanol extracted fraction of yolk, retinol, hemin, yeast extract, broth, farnesol and dolichol fraction of chicken liver. None of these supported growth of *M. lepraemurium.*

"The following neutralizing agents of free radicals were tried in the minimal medium: triethylenediamine, β-carotin, potassium iodide, potassium bromide, 2-aminoethyl-isothiouranium-bromide-hydrobromide and cysteamine. None of these supported growth of *M. lepraemurium*".

34. DELVILLE, J. & JACQUES, P. J. **Effect of treatment** *in vivo* **with Triton WR-1339 and Macrocyclon on infection of the mouse foot-pad by** *Mycobacterium leprae. Biochem. Soc. Trans.,* 1978, v. 6, No. 2, 395–397.

One month after the inoculation of *Mycobacterium leprae* into the footpads of mice, the mice were injected intraperitoneally at weekly intervals with Triton WR-1339 or Macrocyclon in normal saline. The footpads were examined between 41 and 96 days after the start of treatment. With both detergents, the counts of acid-fast bacteria and of granular and solid-stained bacteria were significantly decreased. The results are tabulated. The effect of Macrocyclon was significantly greater than that of Triton.

The authors say that it seems likely, from the viewpoint of final impact on intracellular *Myco. leprae,* that "Triton WR-1339 and Macrocyclon belong in that promising class of antileprotic agents that, like enzymic free-radical and singlet-O_2 generators and yeast glucan, are bactericidal and, in addition, accelerate subsequent intracellular destruction of the parasite."

[See *Trop. Dis. Bull.,* 1978, v. 75, abstr. (1573).]

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35. KOHSAKA, K., MAKINO, M., MORI, T. & ITO, T. **[Establishment of experimental leprosy in nude mice.]** *Jap. J. Bact.,* 1978, v. 33, No. 2, 389–394. [In Japanese.]

"A lepromatoid lesion developed in a nude mouse inoculated with *Mycobacterium leprae* was previously reported by the authors. The secondary passage of *M. leprae* which had proliferated in the lesion of the first infected nude mouse into other nude mice was confirmed experimentally. The reproducibility of animal transmission with nude mice was also proved.

"Successive transmission of *M. leprae* was carried out three times by the foot pad technique with the organism which had proliferated in a nude mouse. *M. leprae* derived from 5 lepromatous patients was also inoculated into foot pads of nude mice. Infected animals were maintained in vinyl (plastic) isolators under an SPF condition.

"Swelling was found microscopically in infected foot pads of all the animals in the 10th month after infection. A lepromatoid lesion was seen at the site of inoculation. At the same time, a bacterial harvest amounted to 3.6×10^8 from a foot pad of the mouse. The nude mouse (BALB/c-*nu/nu*) and its normal littermate (BALB/c-*nu*/+) were examined for body temperature with an electronic thermometer. There was no significant difference in body temperature between the nude mouse and the normal. *M. leprae* was detected from the skin of low-temperatured parts of the body, but not from the skin of high-temperatured parts, in the 10th month after infection. It was seen in lung, liver and spleen, but not in the kidney. *M. leprae* organisms derived from 5 different patients were successfully transmitted into the foot pads of nude mice. The maximum yield of *M. leprae* was 1.1×10^{10} in a foot pad in the 8th month after infection."

36. KAUR, S., KUMAR, B. & GUPTA, S. K. **Fine needle aspiration of lymph nodes in leprosy. A study of bacteriologic and morphologic indices.** *Int. J. Lepr.,* 1977, v. 45, No. 4, 369–372.

In confirmation of a previous study, the morphological indices (MI) of leprosy bacilli in inguinal lymph nodes were found to be higher in most cases than in slit skin smears. Lymph node aspirates were compared with impression smears of excised nodes in 16 cases, and found to give comparable results for both morphological and bacteriological indices. Aspiration of lymph nodes is recommended as a routine bacteriological procedure for leprosy.

[See *Trop. Dis. Bull.,* 1976, v. 73, abstr. 343.]

D. S. Ridley

37. KAWAGUCHI, Y., MATSUOKA, M. & KAWATSU, K. **Pathogenicity of cultivated murine leprosy bacilli of Hawaiian-Ogawa strain in mice. I. The pathogenicity of bacilli from rough colonies.** *Jap. J. Exp. Med.,* 1978, v. 48, No. 1, 17–26.

"This paper deals with the pathogenicity of cultivated murine leprosy bacilli from rough colonies of Hawaiian-Ogawa strain in mice. This strain was isolated by Ogawa, in 1970, on Ogawa's 1% egg yolk medium, from mice previously inoculated with Hawaiian strain of murine leprosy bacilli which has been maintained by passages from mice to mice.

"The pathogenicity of Hawaiian-Ogawa strain was found to belong to the same pattern as Hawaiian strain when the subcutaneous inoculation test was carried out in C57BL/6 and C3H mice, the former being representative of the benign type and the latter being representative of the malignant type.

"In KK mice of the intermediate type with Hawaiian bacilli, however, Hawaiian-Ogawa bacilli produced the lesions with malignant features in almost all the male mice, while the female mice were divided into two groups roughly half showing the intermediate or malignant type. In DDD mice of the benign type with Hawaiian bacilli, some cases of the male mice showed the malignant features, whereas almost all the female mice were of the benign type in the same experimental conditions.

"The pathogenicity of Hawaiian-Ogawa bacilli in mice did not revert into that of Hawaiian bacilli even after serial mouse passage.

"There are slight but definite differences in the mouse pathogenicity between Hawaiian-Ogawa and Hawaiian strains."

38. STANFORD, J. L. *et al.* **A study of alleged leprosy bacillus strain H1-75.** *Int. J. Lepr.,* 1977, v. 45, No. 2, 101–106.

Subcultures of the Skinsnes organism (strain H1-75) cultured from a patient with leprosy were examined bacteriologically in Antwerp and London and identified as a variety of *Mycobacterium*

marianum (syn. *scrofulaceum*). The organism grew on ordinary mycobacteriological media. It gave a skin test reaction in 0/27 patients with tuberculoid leprosy. One of the subcultures also contained numbers of a smaller organism, about the size of *Myco. leprae,* which appeared to be dead. Similar studies of other cultures of the Skinsnes organism must be made to confirm or refute its identity as *Myco. leprae.*

The authors reject the view of Skinsnes and Kato that this organism might be a modified form of *Myco. leprae,* as it differed from it in every way except in being a *Mycobacterium.* It might have been present with the leprosy bacillus in the tissues of the patient since similar organisms have been repeatedly cultured in the past. But they think it most likely to have been a laboratory contaminant.

D. S. Ridley

39. MATSUOKA, M. & KAWAGUCHI, Y. **[Observation of *M. lepraemurium* in subcutaneous tissue of mice by spread tissue preparations.]** *Jap. J. Lepr.,* 1977, v. 46, No. 2, 37–43. [In Japanese.]

"Mice of 6 inbred strains (C3H, CF≠1, BALB/C, KK, DDD and C57BL/6) were inoculated subcutaneously in the back with 0.25 ml of a 1:1000 leproma suspension (Hawaiian strain). Spread tissue preparations were made from the inoculation site at about weekly intervals until 10 weeks to observe growth patterns of murine leprosy bacilli in subcutaneous tissues.

"There were no remarkable differences among these 6 strains during the first 3 weeks after inoculation. In 1 week, an acute inflammatory reaction with polymorphonuclears disappeared and elongation of the bacilli without increase in number was observed in mononuclears. The bacilli showed longer and thinner forms with a length of about 2 to 3 times the initial size. At 3 weeks, enlarged mononuclears, being crowded with the long bacilli, could easily be demonstrable by low magnification.

"Four weeks after inoculation, however, significant differences were observed in growth patterns of murine leprosy bacilli among these mouse strains. In C3H and CF≠1 mice, inflammatory cells consisted mainly of mononuclears, most of which were heavily loaded with the long bacilli. On the contrary, in the other four strains, many lymphocytes and polymorphonuclears were found in the subcutaneous inoculation site, surrounding a smaller number of the bacillus-containing mononuclears. Such differences between mouse strains became more remarkable at 5 weeks, because of more pronounced cellular reactions in these 4 strains.

"The significant differences between C3H and CF≠1 mice were manifested in 10 weeks. In CF≠1 mice lymphocyte infiltration, which surrounded the lesions of mononuclear containing the bacilli, was evident, whereas no host cellular reactions were seen in C3H mice.

"From the results of these observations, this experimental method can be recommended for early evaluation of development of mouse leprosy, with special reference to the relation of the host cells to the organism, and these mouse strain differences are presumably due to the cell-mediated immunity developed in the hosts."

40. MORI, T. **[Cultivation of *Mycobacterium lepraemurium* under low oxygen tensions.]** *Jap. J. Lepr.,* 1977, v. 46, No. 2, 44–47. [In Japanese.]

"Cytochrome b_1 and cytochrome a_2 were detected in the *in vivo* grown or *in vitro* grown *Mycobacterium lepraemurium,* however, cytochrome c and cytochrome a were not found. Cytochrome a_2 is a complex of D and C type cytochrome which is mainly seen in *Pseudomonas aeruginosa* grown in anaerobic condition and is not seen in the bacteria grown in aerobic condition. *Mycobacterium lepraemurium* was grown in aerobic condition on 1% Ogawa yolk medium, however, growing place of the organisms might be fairly anaerobic condition because the cytochrome a_2 was found in this organism. When a few bacteria were inoculated on the 1% Ogawa yolk medium, the organism might be unable to make an optimal anaerobic condition on this medium. Then trial of the cultivation of *Mycobacterium lepraemurium* under low oxygen tension was made by the author.

"Media were put in glass desiccator and were exchanged with gas mixutre through sponge gum cap. Mixture gas was added in desiccator once a week. As shown in Table I, the mixture

gas composed of 5% CO_2, 1% O_2 and 96% N_2 gave the best result for cultivating with a few organisms, but no colony formation was obtained in case of the inoculation with 10^5 bacilli. In the primary isolation of *Mycobacterium lepraemurium* 100% success was not obtained, especially primary isolation from infectious tissue containing relatively little numbers of bacilli was very difficult. As seen in Table 2, the low oxygen condition was better than normal air condition. Primary isolation from ten times diluted inoculum was failed in normal air condition, but succeeded on some tubes in 1% condition. Primary isolation of *Mycobacterium lepraemurium* from tissue culture of A31 cells which contained less bacilli than the murine leproma, is also possible in 1% O_2 condition."

41. MORI, T. **[Cultivation of *Mycobacterium leprae* on modified 1% Ogawa yolk media.]** *Jap. J. Lepr.,* 1977, v. 46, No. 2, 48–51. [In Japanese.]

"Follow-up experiments of Ogawa's method for cultivation of *Mycobacterium lepraemurium* were succeeded by Kozeki and Mori. This steadfast method of isolation of *M. lepraemurium* might have been established today. Now it is urgently necessary that this method should be applied to cultivation of *Mycobacterium leprae* encouraged by the success in case of *M. lepraemurium.* As it was already thought from a biochemical study of *M. lepraemurium* that *M. lepraemurium* might be injured by the excess of oxygen and Prabharan reported that *M. leprae* have a diphenol oxidase and the diphenol might have an important role in the metabolism of *M. leprae,* some suitable reducing agents and diphenol compounds must be used in culture of *M. leprae.*

"Inhibition tests for some reducing agents and diphenol compounds were done by using *M. lepraemurium* and 1% Ogawa yolk medium. As seen in Table 1 and Table 2, the suitable concentrations of DOPA, cystein, thioglycolate and adrenalin were respectively 31γ–62γ, 31γ, 15γ–31γ and 10γ per ml. The other reducing and modified reagents were unsuitable to the growth of *M. lepraemurium.* Then the leproma materials were cultivated for one year at 30°–35°C on 1% Ogawa yolk media modified with 33.3 γ/nl DOPA, 33.3 γ/ml l-cystein, 17 γ/ml thioglycolate and 10 γ/ml l-adrenalin. Eight materials from 8 leprosy patients in National Leprosarium Airakuen, 3 materials from one patient in National Leprosarium Nanseien, one material sent from Professor Nakamura, one material given from National Leprosarium Seishoen and 3 materials from 3 new patients in our clinic were cultured. The results of all experiments were negative even cultivating under the 5% CO_2, 1% oxygen and nitrogen condition."

2. IMMUNO-PATHOLOGY

42. KORANNE, R. V., SINGH, R. & IYENGAR, B. *Mycobacterium leprae* **in the striated muscle of tuberculoid leprosy patients.** *Lepr. India,* 1978, v. 50, No. 3, 375–380.

'Striated muscle specimens from 24 untreated proved cases of tuberculoid leprosy and five healthy normal individuals were studied histopathologically for the evidence of leprous pathology. Atrophy or damage to the muscle fibre was not observed in any patient. Nineteen (79.16%) cases showed evidence of leprosy in striated muscles. Seventeen (70.83%) cases showed scanty histiocytic infiltrate between the muscle fibres. Thirteen (54.16%) cases had acid fast bacilli mostly inside the muscle. There was no correlation between the location of the bacilli and that of the histiocytes; in two cases, acid fast bacilli were seen without the histiocyte. The bacilli were solidly staining and were lying singly in the undamaged muscle. There was no evidence of tuberculosis and, in the Control group, none showed any AFB or infiltrate.

"The presence of lepra bacilli did not depend upon the location of the muscle. Two of the muscle specimens not underneath the cutaneous lesions also had acid fast bacilli. 21.05% of these cases also showed simultaneous involvement of liver and lymph nodes. These are strong evidence of systemic nature of disease in tuberculoid leprosy as well."

43. AGARWAL, S. K. & SAHA, K. **Serum alpha-1-antitrypsin in various forms of leprosy.** *Indian J. Med. Res.,* 1978, v. 68, July, 136–139.

"Serum alpha-1-antitrypsin (AAT) levels were estimated by single radial immunodiffusion technique using monospecific antiserum in 55 patients with various forms of leprosy and compared with its levels found in 60 healthy controls and 50 patients with chronic obstructive airway disease (COAD). Although progressive increase in serum AAT level was observed from normal controls (225±84 mg per cent) through tuberculoid (236±67) to lepromatous (247±95) leprosy patients, a significant elevation was noticed only in cases complicated with ENL (351±97). On the contrary, the patients with COAD demonstrated a significant decline (183±73) of serum AAT. It has been postulated that AAT is an acute phase reactant and is released during the reactive phase of the illness to counteract various endogenous as well as exogenous proteases."

[See also *Trop. Dis. Bull.,* 1977, v. 74, abstr. (832).]

See also DELIA *et al.,* abstr. 3132; DUTTA and DUTTA, abstr. 3134.

44. MINAGAWA, F., YOSHINO, Y. & ABE, M. **Early immune responses in nude mouse following intravenous injection of** *Mycobacterium leprae. Jap. J. Lepr.,* 1978, v. 47, No. 1, 37–42.

"For the purpose of elucidating immune mechanism in early stage of leprosy, three strains of mice, conventional BALB/c, SPF BALB/c-*nu*/+ and BALB/c-*nu*/*nu* mice, were injected intravenously with a mixture of 10^7 *M. leprae* and 10^8 sheep red blood cells. All of these mice showed similar degree of antibody response to *M. leprae,* as demonstrated by indirect immunofluorescence, the antibody-*titer* reaching to the maximum within a week after the injection of antigens. The production of IgG antibodies was somewhat delayed and the *titer* reached to a plateau within 2 or 3 weeks. No decline of antibody-*titer* was observed till at least 5 weeks after the injection of antigens. The transfer of thymocytes from immunized *nu*/+ donors to *nu*/*nu* recipients did not influence the antibody-*titer* in the recipient."

45. JOB, C. K., CHACKO, C. J. G. & TAYLOR, P. M. **Electronmicroscopic study of histoid leprosy with special reference to its histogenesis.** *Lepr. India,* 1977, v. 49, No. 4, 467–471.

Biopsy specimens of histoid nodules from 2 patients were examined by electron microscopy. The thin, elongated histoid cells were found to be closely invested by collagen fibrils. Many small finger-like villi were present on the cytoplasmic surface, mitochondria and lysosomes were numerous and rough endoplasmic reticulum was increased. Thus the cells shared the features of both macrophages and fibroblasts. Numerous bacilli were present, both in phagolysosomes and outside them, but electron transparent substance, or foam, was relatively scanty. It was concluded that the histoid cells were histiocytes, and that the differences from the cells in ordinary lepromatous lesions were due to local proliferation of the cells in response to stimulation by rapid multiplication of *Mycobacterium leprae.* Ordinarily macrophages accumulated by the infiltration of monocytes from the blood.

D. S. Ridley

46. GUPTA, J. C., PANDA, P. K., SHRIVASTAVA, K. K., SINGH, S. & GUPTA, D. K. **A histopathological study of lymphnodes in 43 cases of leprosy.** *Lepr. India,* 1978, v. 50, No. 2, 196–203.

47. BAPAT, C. V., MODAK, M. S., DESOUZA, N. G. A. & CHULAWALLA, R. G. **Comparative study of skin reactions in leprosy patients to** *M. leprae*-**lepromin and to ICRCin, an antigen from cultivable acid-fast bacilli from** *M. leprae* **isolated from lepromatous nodules.** *Lepr. India,* 1977, v. 49, No. 4, 472–484.

"Skin test antigens (Dharmendra type) were prepared from fresh *M. leprae* (lepromin) and from a culture of strain C-44 ICRC bacilli (ICRCin) grown *in vitro* from *M. leprae* isolate from

lepromatous nodules. Comparative study of skin reactivity to lepromin and ICRCin—both 'early' and 'late' reactions in 76 leprosy patients was conducted. In 29 lepromatous (LL) cases, 25 exhibited totally negative reaction at the end of the third week. In tuberculoid (TT) 22 and 23 out of 31 were positive (> 4.5 mm) at 3 weeks to lepromin and ICRCin respectively. In the 16 BB group, the reactions were comparable in the same patient. The cellular reaction in tuberculoid cases consisted of lymphocyte infiltration, epitheloid giant cells and Langhan type cells and indistinguishable from each other. These data with characteristic total lack of reaction in 25/29 lepromatous leprosy cases and identical cellular reaction in TT patients, provide strong evidence that ICRC bacillus strain C-44 is antigenically identical with *M. leprae*."

[The "ICRC bacillus" is not a single strain, but consists of a number of isolates of a cultivable *Mycobacterium* obtained from different human lepromas. Its full antigenic profile is currently being studied and results are awaited. The present paper indicates that it is antigenically closely related to *M. leprae,* but it is overstating the case at this stage to claim that it is "antigenically identical with *M. leprae*", because:— a) only Dharmendra and no Wade-Mitsuda type antigen was studied; b) lepromatous patients nos 10, 24 and 53 gave discordant early reactions and patient no. 26 gave a discordant late reaction, the latter being particularly important; c) no biopsies were taken of lepromatous reactions.]

M. F. R. Waters

48. SERJEANTSON, S. & WOODFIELD, D. G. **Immune response of leprosy patients to hepatitis B virus.** *Am. J. Epidem.,* 1978, v. 107, No. 4, 321–327.

The immune responses to hepatitis B virus of 323 Melanesian patients with leprosy in Papua New Guinea and 290 control subjects were studied using sensitive assay techniques. It was found that patients with lepromatous leprosy, whether in institutions or not, tended to have the highest rates of hepatitis B surface antigen and were significantly different from the patients with the tuberculoid form of leprosy. In the multivariate analyses of antigenaemia, severity of the disease remained a significant determinant of the rates of surface antigen. Similarly, when the series was grouped into three immune response categories of surface antigen, surface antibody or no serological evidence of exposure to hepatitis B virus, the severity of leprosy was a significant factor in determining the immune response. For lepromatous and borderline lepromatous patients, the probability of responding antigenically to the virus, given that some measurable response has occurred, is 0.420. The corresponding probability for tuberculoid patients is 0.250 and for healthy control subjects 0.293. These probabilities suggest that the lepromatous patients have an impaired immune response that not only predisposes them to the most severe form of leprosy but also decreases their efficiency in terminating hepatitis B infection with surface antibody. In contrast, patients with tuberculoid leprosy are as efficient as healthy control subjects in mounting an antibody response.

A. J. Zuckerman

49. JOB, C. K., KIRCHHEIMER, W. F. & SANCHEZ, R. M. **Liver lesions in experimenta lepromatoid leprosy of the armadillo. A histopathologic study.** *Int. J. Lepr.,* 1978, v. 46, No. 1, 1–8.

"A retrospective study of liver lesions was made in 13 armadillos infected intracutaneously with 10^7 *M. leprae* from the same inoculum, to evaluate the pathogenesis of the experimental disease. Survival times ranged from 13 to 55 months. In seven armadillos the liver lesions were markedly less severe than in six of these animals. The extent of the lesions was unrelated to the duration of the infection and was interpreted as reflecting individual differences in resistance. In contrast to man, leprosy bacilli were found in the liver cells of both groups of armadillos but to a lesser extent in those of the more resistant armadillos. The latter also had no obvious changes in the liver tissue except for round cell infiltration and prominent Kupffer's cells which contained *M. leprae*. These lesions can be compared to indeterminate leprosy in humans.

"The lesions in the more susceptible (lepromatoid) armadillos were initiated in Kupffer's cells. Later, large collections of bacillated macrophages infiltrated the liver lobules. The liver cells

heavily loaded with *M. leprae* developed a pale granular cytoplasm which became foamy in the late lesions. In three of the lepromatoid livers, lesions compatible with *erythema nodosum leprosum* were seen."

50. NUTI, M., TARABINI, G. C., TARABINI, G. C. L. & THAMER, G. L'antigene *e* (HB_eAg) nella lebbra. [**The *e*-antigen in leprosy.**] *Quad. Sclavo Diagn.*, 1977, v. 13, No. 4, 393–403. English summary.

From a consideration of all the data so far collected by various workers, it can be said that the occurrence of HB_sAg does not differ between lepromatous and tuberculoid leprosy patients, nor does the occurrence differ from that in the rest of the population, though there is a positive correlation between this incidence and the climatic and environmental conditions of the groups studied, HB_sAg being more frequent in patients mostly deriving from tropical countries and closed communities, on whom most of these observations were made. The investigation here reported deals with the incidence of HB_eAg, this antigen being said to be in direct and close relation with infectivity and with the persistence of the B virus in the circulation.

Sixty-six samples of serum from 42 patients with lepromatous and 24 with tuberculoid leprosy, in Somalia, were examined. For HB_sAg and its antibody were radioimmunologically assayed and the Ouchterlony immunodiffusion method was used for HB_eAg and its antibody. HB_eAg was not found in any case; HB_eAb was found in 3 cases of lepromatous leprosy. HB_sAg was found in 10 cases of lepromatous and in 3 of tuberculoid leprosy. HB_s antibodies were found in 16 cases of lepromatous and in 10 cases of tuberculoid leprosy. The 3 patients with HB_eAb also carried HB_sAg. There was no relation with age or sex. The absence of HB_eAg suggests that these carriers present a low degree of risk or none at all. It appears persons with a depressed cell-mediated immunity reaction tend to acquire the B virus antigen more easily and with more difficulty to show the corresponding antibody.

E. Agius

51. POULTER, L. W. **Systemic immunological reactivity in the absence of delayed type hypersensitivity during murine leprosy.** *Cellular Immunol.*, 1978, v. 40, No. 1, 117–127.

"The generation of cell-mediated immunological reactivity has been examined following systemic infection of mice with *M. lepraemurium* (MLM). It has been found that although delayed-type hypersensitivity to MLM is ablated within 2 weeks of infection, resistance, as determined by a containment of the multiplication of the organism at various sites, persists for at least 7 weeks. During this time it was found that a population of lymphocytes sensitized to MLM antigens appeared within these animals and that DTH could be generated if these cells were focused at a footpad site.

"The possibility that these changes in immunological status are determined by increasing levels of antigen, resulting from a systemic killing of MLM is discussed. It is postulated that persistent desensitization eventually results in anergy to MLM."

52. SAHA, K., SARIN, G. S., CHAKRABORTY, A. K. & SEN, D. K. **Ocular immunoglobulins in lepromatous leprosy.** *Int. J. Lepr.*, 1977, v. 45, No. 4, 338–342.

"Immunoglobulin levels in the ocular fluids have been estimated in normal subjects and lepromatous leprosy patients. In the normal tear, IgA is the major immunoglobulin while IgG is the only immunoglobulin detected in the aqueous humor. The immunoglobulin profiles in the tear and the aqueous humor in normal subjects are different. The mean IgA level in the tears of the lepromatous leprosy group is significantly lower than in the control patients. IgA and IgG levels are raised in the aqueous humor of some leprosy cases who had suffered from uveitis in the past and also in all cases with active endogenous uveitis. Therefore, in lepromatous leprosy the pattern of immunoglobulin alteration in the tear and the aqueous humor is not parallel."

53. OKADA, S., KOMURA, J. & NISHIURA, M. *Mycobacterium leprae* **found in epidermal cells by electron microscopy.** *Int. J. Lepr.,* 1978, v. 46, No. 1, 30–34.

"Leprosy bacilli were found in a keratinocyte of the epidermis by the electron microscopic observation of the ultrathin section of a leproma. The possibility of discharge of leprosy bacilli from the skin should be considered even if the lepromatous patient does not have any ulceration."

54. SAOJI, A. M. & MENE, A. R. **Persistence of Australia antigen in leprosy — a frustrating puzzle in immunology.** *Lepr. India,* 1978, v. 50, No. 1, 7–10.

Hepatitis B surface antigen was detected by the electro-immunodiffusion technique (Laurell's rocket method) in the serum of 4% of 100 patients with lepromatous leprosy and in 2% of 100 patients with tuberculoid leprosy or with a positive lepra reaction in India. Surface antibody was found in 3% of the patients with lepromatous leprosy.

A. J. Zuckerman

55. SASIAIN, M. C., CAROSELLA, E. D., BALINA, L. M., BREZAVSCEK, D. M. & BACHMANN, A. E. **A study of cellular and humoral immunity in three species of armadillos. Part I.** *Int. J. Lepr.,* 1977, v. 45, No. 4, 323–326.

"In the present study the membrane receptors of immunocompetent cells and immunoglobulins in three varieties of armadillos were explored for determining, in later studies, the possible differences in inoculated animals developing leprosy. The studies of cellular immunity were performed in five *Chaetophroctus villosus* (Ch.v), one *Dasypus hibridus septecinctus* (DHS) and one *Zaedus pichei* (ZP), while the humoral immunity was studied with a serum pool of 17 Ch.v and 6 DHS. The results obtained demonstrate that the lymphocytes of the three species studied have receptors for SRBC, C3 and Ig-s, and no receptors for Fc segment of immunoglobulins. With reference to immunoglobulins no definite alteration of the humoral immunity was observed with the exception that DHS presents increased IgG levels and Ch.v increased IgM."

3. CLINICAL

56. EKAMBARAM, V. & SITHAMBARAM, M. **Self-healing in non-lepromatous leprosy in the area of the ELEP Leprosy Control Project Dharmapuri (Tamil Nadu).** *Lepr. India,* 1977, v. 49, No. 3, 387–392.

Six years' observation of 432 patients with non-lepromatous leprosy, most of them presenting single lesions, and none of them taking chemotherapy, revealed that self-healing occurred in 72.92%; 20.8% remained stationary; and only 6.25% became worse.

T. F. Davey

57. HANSENOLOGIA INT., 1977, v. 2, No. 1, 94–98. Associação de hanseníase e periarterite nodosa. [**Association of leprosy with periarteritis nodosa.**] English summary.

58. BARNETSON, R. StC. & BRYCESON, A. D. M. **Cutaneous leishmaniasis and leprosy.** *Trans. R. Soc. Trop. Med. Hyg.,* 1978, v. 72, No. 2, 160–163.

"Eight patients who had concomitant leprosy and leishmaniasis are described. Two patients with lepromatous leprosy had high resistance leishmaniasis, implying that immune deficiency in lepromatous leprosy is specific to *Mycobacterium leprae*."

59. DATAR, S. V., PANSARE, M. S. & KATTI, V. A. **Leprosy and ABO blood groups.** *Lepr. India,* 1978, v. 50, No. 3, 388–391.

"Two hundred and fifty patients with lepromatous and non-lepromatous leprosy were studied. The statistical analysis showed that there is no relationship between the blood groups and lepromatous or non-lepromatous leprosy. The results are discussed in comparison with the work of other authors."

60. KORANNE, R. V., SINGH, R. & IYENGAR, B. **Bone-marrow in tuberculoid leprosy.** *Lepr. India,* 1978, v. 50, No. 2, 181–184.

"Twenty-four untreated patients with proved tuberculoid leprosy and five healthy controls were investigated for the involvement of bone-marrow. The cytology was essentially normal and no acid-fast bacilli was seen in the bone-marrow smears."

4. THERAPY

61. MATSUO, Y., UTSUNOMIYA, S., KAJIHARA, N. & KIM, S. K. **Combinations of rifampicin and isoprodian in the treatment of *Mycobacterium leprae* infections in mice.** *Jap. J. Lepr.,* 1978, v. 47, No. 1, 43–47.

"Combinations of rifampicin and isoprodian were tested against *Mycobacterium leprae* in mice. Drugs were given by gavage once daily, 6 times per week, starting from the day of infection to day 21 after infection in the first experiment, and from day 51 to day 80 after infection in the second experiment. Although a few combinations had some increases of the growth delay over single drugs, it is not likely that appreciably additive effect of both drugs has been noticed in the treatment of *M. leprae* infections in mice."

[Isoprodian is a combination of isoniazid, prothionamide and dapsone. See also *Trop. Dis. Bull.,* 1976, v. 73, abstr. 352.]

62. NOORDEEN, S. K. **Long term effects of chemoprophylaxis among contacts of lepromatous cases. Results of an $8\frac{1}{2}$ years follow-up.** *Lepr. India,* 1977, v. 49, No. 4, 504–509.

An $8\frac{1}{2}$-year follow-up after the termination of a controlled study of chemoprophylaxis with dapsone involving 700 children revealed that those who received dapsone continued to show a degree of protection superior by 56.1% compared with children who received a placebo. This protection was seen about equally in all age-groups, and it was much higher among males than among females. Chemoprophylaxis was more effective in the $2\frac{1}{2}$ years after termination of treatment than in later periods. It is suggested that this "carry over" benefit from chemoprophylaxis might be caused by the drug aborting subclinical infections without interfering with the development of immunity.

T. F. Davey

63. BALAKRISHNAN, S. **Monitoring self administration of dapsone by patients.** *Lepr. India,* 1977, v. 49, No. 3, 364–371.

"The urinary DDS/creatinine ratios in the supervised in-patients and out-patients attending the C.L.T. & R.I. clinic were compared. The subjects of this study were receiving dapsone at the daily dosage of 25, 50 and 100 mg or bi-weekly dosage of 25, 50, 75, 100 and 200 mg. The mean urinary DDS/creatinine ratios from out-patients were significantly lower than those of the in-patients in both dosage schedules of treatment and suggest that a certain percentage of out-patients have been irregular in the intake of dapsone in the period immediately prior to the collection of urine specimens. The estimated percentage of gross irregularity of intake is

markedly higher in the bi-weekly as compared with the daily dosage schedule. The gross irregularity of intake was particularly marked in the higher dosage groups such as 100 mg daily or bi-weekly and 200 mg bi-weekly. The implications of the findings are discussed."

64. NAIK, S. S. & PANDYA, S. S. **Dapsone in wheat flour as a possible method of therapy in leprosy. A laboratory report.** *Lepr. India,* 1977, v. 49, No. 4, 516–520.

Dapsone tablets were added to wheat, in the proportion of 400 mg dapsone to 1 kg wheat, and ground in the flour mill. The flour was used for 2 weeks by a family for cooking chapatties and no change in taste was reported. Blood and urine levels of dapsone were comparable to an intake in adults of 50 to 100 mg dapsone daily. [The problems inherent in administering dapsone by this method are not discussed.]

M. F. R. Waters

65. IYER, C. G. S., BALAKRISHNAN, S. & RAMU, G. **A comparison of low and conventional dosages of dapsone in the treatment of lepromatous leprosy.** *Lepr. India,* 1977, v. 49, No. 3, 372–386.

"A therapeutic trial using two dosages of dapsone with a schedule of administration of the drug once a week was undertaken at the Central Leprosy Teaching and Research Institute, Chingleput. Adult males with active lepromatous leprosy who were either previously untreated, or who had no specific treatment for at least three months immediately prior to their inclusion into this study, were the subjects of this trial. Two dosages, viz., 10 mg per kg body weight/week, and 3.3 mg per kg body weight/week, were employed in this trial.

"It was found that dapsone administered orally as a single dose once a week was therapeutically effective in most of the patients, and improvement, clinical or bacteriological, was directly related to the duration of treatment, irrespective of the dosage of dapsone. Blood levels of dapsone in these patients were in general commensurate with the dose of the drug in either group. No adverse effects on any of the visceral functions were encountered during the prolonged use of this schedule of treatment with dapsone."

66. GIRDHAR, B. K., SREEVATSA & DESIKAN, K. V. **Primary sulphone resistance: a preliminary report.** *Lepr. India,* 1978, v. 50, No. 3, 352–355.

"A case of lepromatous leprosy proven to be a primary sulphone resistant one, has been reported. Bacilli from the case were found to be resistant as checked by their continued growth in the foot pads of mice receiving diet containing 0.001% DDS. A study to identify such cases is being systematically pursued."

67. PANDYA, N. J. **Surgical decompression of nerves in leprosy. An attempt at prevention of deformities. A clinical, electrophysiologic, histopathologic and surgical study.** *Int. J. Lepr.,* 1978, v. 46, No. 1, 47–55.

"Forty-five leprosy patients were electively subjected to extraneural decompression and medial longitudinal epineurotomy in anticipation that relief from compression may favorably alter the course of the disease by retrieving reversibly damaged nerve bundles and preventing further progression of disease. Neurolysis was performed in 69 nerves, including the ulnar, median, lateral popliteal and posterior tibial. The period of follow-up was up to three years. Excellent sensory recovery was seen in most patients while motor recovery was less predictable. The recovery seen was better in those patients taking treatment early and also at the age the surgery was carried out. Motor damage appeared more severe in the 10–20 year age group. Most of the beneficial effects can be explained on the basis of increased vascularity due to relief from extraneural and intraneural compression."

5. EPIDEMIOLOGY

68. GANAPATI, R., PANDYA, S. S., NAIK, S. S., DONGRE, V. V. & DESOUZA, N. G. A. **Assessment of school surveys as a method of case detection in an urban area endemic for leprosy.** *Indian J. Med. Res.,* 1977, v. 66, No. 5, 732–736.

"The study was conducted to determine whether school survey and examination of family contacts was an effective method of case detection in a community where leprosy is endemic as compared to whole population survey. The results showed that although school and family contact examination was more economical as regards time, money and personnel involved, it did not result in the identification of a significant number of cases in the community, either in numbers or in the proportion of infectious cases. This observation implied that most children detected to have leprosy in the school were infected from sources outside the home. The whole population survey revealed a serious shortcoming in that only 60 per cent of the adult male group was covered, a lacuna which is of potential epidemiologic importance."

69. KAPOOR, P., DEODHAR, N. S. & YELLAPURKAR, M. V. **Integration of leprosy control work with general health services as planned in Maharashtra.** *Hlth Popul.,* 1978, v. 1, No. 1, 51–61.

"The current literature on integration of Leprosy Control work with General Health Services has been reviewed. In view of the introduction of Multipurpose Workers' Scheme and an experience in a pilot project, the authors feel that the time of integration of leprosy is ripe. The process of involvement of Multipurpose Workers in the Leprosy Control Programme is being introduced in a manner that ensures adequate supervision by the present Leprosy Control staff during the training period and also subsequently for one year so that the transition from unipurpose to integrated service is a smooth one. After the successful integration of leprosy, the leprosy staff, after adequate training, can be used as Multipurpose Supervisors."

70. SAIKAWA, K. [**The epidemiological study on leprosy in the Ryukyu Islands. The 5th report: on leprosy in the urban area.**] *Jap. J. Lepr.,* 1977, v. 46, No. 1, 8–13. [In Japanese.] English summary.

In the main island the leprosy prevalence rate and the leprosy incidence rate were, respectively, 1.34 and 0.059 per thousand in 1975 compared with 1.97 and 0.088 in 1970. However, in Naha City on the Okinawa mainland (population about 300,000) 20 new cases were detected in 1974 compared with only 5 in 1969. In a rural area, in the Miyako Islands (population 69,000 in 1969, 58,000 in 1974), 17 cases were found in 1974 whereas there were 38 in 1969. Further information is provided in tables and figures.

F. I. C. Apted

71. SAIKAWA, K. [**The epidemiological study on leprosy in Okinawa Island. The third report; on the islets.**] *Jap. J. Lepr.,* 1977, v. 46, No. 1, 1–7. [In Japanese.] English summary.

Tables, in English, show the numbers of new cases of leprosy reported on each of 11 islands in the Okinawa archipelago for each 5-year period from about 1936 to 1975. In 7 of the islands leprosy notifications have remained at a low level — nearly all single figures for each 5-year period — over the whole of this time. In the other 4 islands the situation is different. In Kume and Irabu islands some 25–35 new cases have been reported in most of the more recent 5-year periods, and in Yonaguni about 10–15 cases. There were fewer notifications from Tarama Island, but in each of these 4 islands the proportions of lepromatous cases and of infected children are high. Graphs show the leprosy incidence rate, lepromatous ratio, and child ratio for each of 8 islands.

F. I. C. Apted

72. HONEY, N. R. **Leprosy in Hong Kong, past, present and future.** *Bull. J. Soc. Community Med. Hong Kong,* 1978, v. 9, No. 1, 22–28.

"During the past two decades, the incidence of leprosy declined from a peak of 16.2 per 100,000 population in 1956 to a low level of 1.7 per 100,000 population in 1976. The decline appears to be associated with the use of specific antileprotic drugs, improved socio-economic conditions and migration patterns. During the period segregation of patients has almost ceased and management of patients is now based on the knowledge that bacteriologically positive patients become non-infectious after a short period of treatment."

73. LECHAT, M. F., VELLUT, C., MISSON, C. B. & MISSON, J. Y. **Application of an economic model to the study of leprosy control costs.** *Int. J. Lepr.,* 1978, v. 46, No. 1, 14–24.

"The effectiveness of various control methods for reducing the incidence of leprosy have been tested over 20 years and compared with predictions made using the present current control method (early diagnosis and mass treatment). Specific vaccination of the whole population, a control measure yet to be developed, has been identified as the most effective strategy in the long run.

"A cost-effectiveness analysis has been carried out for three indicators, annual incidence, annual prevalence and cumulative prevalence at 20 years, using cumulative costs. The analysis indicates that specific vaccination at high levels of coverage is the most effective method for controlling incidence in the long term. Provided the cost of the vaccination campaign during the first years (roughly fourfold the funds required for carrying out the current strategy) can be supported, specific vaccination is also the most cost-effective method where a high level of effectiveness is required. Specific vaccination is still the most advantageous method if prevalence or cumulative prevalence are taken to indicate the effectiveness of leprosy control. The BCG-type of vaccination is not only less effective, but is also less cost-effective.

"Reducing the rate of abandonment of treatment (which in the model has been simulated by increasing the rate of resuming treatment) and earlier detection both appear as useful methods under conditions of severe budgetary constraints. Their ultimate effectiveness in terms of incidence reduction is, however, very small. As expected, segregation is costly and ineffective compared with other methods.

"In each simulation, the cost of treating the backlog of patients already ill or infected (incubating) at the time the control measures are initiated is high. Methods aimed at reducing transmission, such as vaccination, early treatment or segregation, have long-delayed effects on the cost even if incidence is reduced. The major cost item in these control measures is the prolonged or even life-long treatment of patients.

"The development of fast-acting, effective treatment is likely to be the only way to reduce the cost in the short term. Thus, in addition to research aimed at developing a vaccine for leprosy, resources should also be allocated for developing new therapeutics."

74. NASSERI, K. & KO, Y. H. **Epidemiology of leprosy in Iran.** *Int. J. Lepr.,* 1977, v. 45, No. 4, 355–359.

"A total of 907 cases of leprosy from two sources, records from Baba-Baghi Leprosarium (709 cases) and Ahar case finding survey (198 cases), have been studied. The main characteristics of the cases are: (a) about 50% of all cases are lepromatous leprosy; (b) the leprosarium cases are about 2.5 years younger; (c) about 70% of all cases are male; and (d) the incidence of leprosy shows a steady increase up to 25–30 years of age and levels off thereafter. These and other findings are discussed."

75. NIGAM, P., VERMA, B. L. & SRIVASTAVA, R. N. **Leprosy — a clinicoepidemiological study in a rural population of Bundelkhand.** *Lepr. India,* 1977, v. 49, No. 3, 349–359.

An epidemiological survey for leprosy in a rural area of north India revealed a prevalence rate of 5.41 per thousand, most cases being in an early stage, and 7 of the 18 cases found being of the

lepromatous type. Ninety-one per cent of the people were examined. These facts, combined with the non-acceptance by the community of persons with advanced leprosy, suggest that the true prevalence of the disease is probably higher than the findings indicate. The disease presented no unusual features.

T. F. Davey

76. WKLY EPIDEM. REC. 1978, v. 53, No. 20, 147. **Leprosy.** [In English and French.]

1832 cases of leprosy were reported in Bolivia in 1977. Of these, 855 were notified from the Department of Santa Cruz, and the remainder, in approximately equal numbers, from Beni and Chuquisaca. Of the total cases, 807 were of the lepromatous type, 561 tuberculoid, 303 indeterminate, and 161 borderline. The total number of cases in the country is estimated at 3907, a prevalence of about 1 per 1000 inhabitants. In the three Departments mainly affected surveillance is carried out by a total of 5 leprologists, in another Department it is undertaken by a dermatologist and elsewhere in the country by the provincial medical officers.

F. I. C. Apted

6. MISCELLANEOUS

77. LEPR. INDIA, 1977, v. 49, No. 3, 440–447. **The WORTH Trust. A report on their activities.**

Formerly known as the Swedish Red Cross Rehabilitation Industries, Katpadi, the WORTH (Workshop for Rehabilitation and Training of the Handicapped) Trust manages 4 rehabilitation institutions for leprosy sufferers and others with disabilities. These provide training in light engineering. The report concludes thus:

"The conviction of the Swedish Red Cross, and the determination with which they pursued the cause under difficult conditions, when very little was done in this area, has amply been rewarded by the success of the project . . . It is the belief of the Worth Trust that a centre run for the physically handicapped with no Governmental or private grants can succeed as a business venture. As a humanitarian effort, it has brought relief and solace to over three hundred handicapped persons. Hardworking wage earners, they do not live on charity, but are skilled workmen who pay taxes, and support families."

T. F. Davey

78. PHILLIPS, M. A. **Health education in leprosy: the problem of overcoming fear and misconceptions.** *Int. J. Hlth Educ.,* 1978, v. 21, No. 2, 130–136.

The author, now in leprosy control work in Lesotho, was in Uganda from 1965 to 1976 where she helped to develop the rehabilitation section of Kumi Leprosy Centre. There are 12 references, concerned with East Africa and Ethiopia in particular but of wide significance.

79. LEPR. INDIA, 1977, v. 49, No. 3, 448–452. **Pune Urban Leprosy Investigation Centre. Report for the period April 1975 to December 1976.**

A series of tables summarizes progress made in the Urban Leprosy Control Project in Poona. These include: cases of leprosy found by survey and by voluntary reporting, statistics of treatment and disabilities, and information on a very active health education programme. Urban leprosy control presents many difficulties and the details given are of interest.

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