

## Abstracts.

### 1. MICROBIOLOGY

1. SKINSNES, O. K., MATSUO, E., CHANG, P. H. C. & ANDERSSON, B. *In vitro* cultivation of leprosy bacilli on hyaluronic acid based medium. 1. Preliminary report. *Int. J. Lepr.*, 1975, v. 43, No. 3, 193-203.

Recent studies by the authors have indicated that hyaluronic acid might be an essential metabolite for *Mycobacterium leprae*, and one which enhances the multiplication of the organism in the mouse abdomen\*. They now apply these findings to the cultivation of *M. leprae in vitro* using a liquid medium (LA-3) based on hyaluronic acid with the addition of yeast extract, bovine albumin, glycerine and phosphate buffer; and also a solid medium (LA-3p) with similar ingredients plus agar. These media were inoculated with organisms from 4 patients with untreated lepromatous leprosy (one in relapse) and from 2 mouse abdominal walls. All strains of bacilli from the above sources grew well on the LA-3 medium except that one was lost by contamination. Initial growth was observed after 2 to 6 weeks. The authors identify the cultured organism as *M. leprae* for the following reasons:

(1) Pathologic and experimentally determined rationale for the essential *M. leprae* nutrient requirement.

(2) Several cultures having the same characteristics have been isolated from LL patients widely separate in time and by geography.

(3) Failure of culture isolates to subculture on the usual media employed in the cultivation of mycobacteria at both 37°C and room temperature.

(4) 1° cultures in liquid medium successfully transferred to 2° liquid medium and to 2° agar medium plates.

(5) Bacillary isolates and bacilli of 1° and 2° liquid medium cultures, as well as LA-3P cultures, all stain with pooled LL serum, FITC coupled, *M. leprae* specific antibody with which a broad range of other mycobacteria do not react.

(6) *M. lepraemurium* also presents good growth on this medium.

This is a very important claim, and the authors are clearly convinced of its veracity. However, there are a number of surprising facts to be taken into account which indicate that, if the new organism is *M. leprae*, then the orthodox view of *M. leprae* is almost wholly at fault. The organism whose growth in mice is promoted by hyaluronic has a partly extracellular habitat. It does not require a cool tissue site and its *in vitro* culture temperature is 37°C. Its growth is faster than would be expected from experience of leprosy in mice. On first isolation it is non-acid-fast and shows suggestions of branching, and only after about six weeks is it predominantly acid-fast. It gives specific immunofluorescence only during the early non-acid-fast phase; by 3 weeks it is negative. Results with the electron microscope tellurite viability test indicate that it is the non-acid-fast phase that is viable, whereas well-stained acid-fast forms may not be viable. These rather revolutionary results deserve some caution pending their confirmation, which it is hoped will be forthcoming.

D. S. Ridley

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\* Matsuo *et al.* *Int. J. Lepr.*, 74, 42, 399 and 75, 43, 1.

2. STORRS, E. E., WALSH, G. P. & BURCHFIELD, H. P. Development of leprosy in another species of armadillo *Dasypus hybridus* (L.); genetic and immunologic implications. *J. Trop. Med. Hyg.*, 1975, v. 78, Nos 10/11, 216-218.

The development of severe disseminated leprosy in one of a pair of seven-banded armadillos (*Dasypus hybridus*) after inoculation with *Mycobacterium leprae* is reported. This is a smaller animal than the nine-banded armadillo, but is of interest in that it regularly produces 8-16 monozygous young, compared with 4 in the case of its larger relative. This feature gives *Dasypus hybridus* a potential importance in studying the relationship of susceptibility in leprosy to genetic factors.

T. F. Davey

3. CLOSS, O. Experimental murine leprosy: growth of *Mycobacterium lepraemurium* in C2H and C57/BL mice after foot-pad inoculation. *Infection & Immunity*, 1975, v. 12, No. 3, 480-489.

Forty-three female C57/BL and C3H mice were inoculated with  $2.7 \times 10^6$  *Mycobacterium lepraemurium* into each hind footpad. The foot thickness and the number of acid-fast bacilli in the footpad and popliteal and inguinal lymph nodes were recorded. In addition the morphological index and the mean bacillary length were determined in the footpad and in the popliteal lymph node. The bacilli multiplied in both strains during the first 4 weeks after inoculation. After that time no further increase in acid-fast bacilli was observed in the C57/BL strain; the bacilli became elongated and the morphological index decreased. These changes were preceded by a local swelling of the footpad due to the onset of an immune reaction. Thus, under the present conditions, C57/BL mice were able to resist experimental infection with *M. lepraemurium* by developing an immune response. In C3H mice no indication of an immune reaction was detected, and the bacilli continued to multiply throughout the observation period. The mouse footpad model seems to provide an excellent basis for the use of experimental murine leprosy to study immunity to mycobacterial infections. Certain aspects of the present model are discussed in relation to the mouse footpad model as used in the study of *M. leprae* infection in mice.

4. STANFORD, J. L *et al.* Preliminary taxonomic studies on the leprosy bacillus. *Br. J. Exp. Path.*, 1975, v. 56, No. 6, 579-585.

Antigens extracted from leprosy bacilli obtained from infected human and armadillo tissues have been examined by immunodiffusion analysis with serum samples from lepromatous patients and with immune sera raised in rabbits. Using the best combinations of serum and antigen extracts, 12 antigenic constituents were found in the leprosy bacilli. Six of these were antigens common to all mycobacteria and nocardiae, 4 were specific to the leprosy bacillus and the position of 2 could not be determined. Groups ii and iii antigens (i.e. those associated with the slow growing and fast growing subgenera of mycobacteria) were not found in the leprosy bacillus, suggesting some relationship with *M. vaccae* and similar strains, in which these antigens are also missing. Lymphocyte transformation tests performed on lymph node cells of mice infected or immunized with leprosy bacilli also showed the leprosy bacillus to have a closer relationship with *M. vaccae* than with other mycobacteria.

5. PRABHAKARAN, K. A survey of attempts at cultivation of *Mycobacterium leprae* *in vitro* and experimental transmission of leprosy to animals. *Lepr. India*, 1975, v. 47, No. 4, 325-336.

A selected survey is made of repeated efforts over the past 100 years at cultivation of *Myco. leprae* in chemically defined media and in tissue cultures. It is pointed out that none of the

claims of success on continued cultivation of the bacilli *in vitro* has been corroborated by other workers. Attempts to transmit human leprosy to experimental animals are reviewed. Except for the nine-banded armadillos (which have a limited geographic distribution and which have so far not been bred in captivity), no other species of animals has been found to be naturally susceptible to the systemic form of the disease.

[There are 74 references, but these do not include those to some of the early work mentioned in the text.]

6. GANAPATI, R. & CHULAWALA, R. G. **Bacteremia in leprosy and its relation to distribution of *M. leprae* in skin.** *Lepr. India*, 1976, v. 48, No. 1, 42-47.

Evidence of bacillaemia through examination of heparinized blood smears was obtained in 17 of the 20 cases (85%) of untreated leprosy cases belonging to the spectrum ranging from BT to LL. Among 17 cases whose blood smears were positive for AFB, the endothelial cells of blood vessels in skin lesions showed AFB in 11 instances (64.7%) and in 7 (41.2%) of these cases biopsies obtained from apparently normal skin also showed bacilli in the blood vessels. The fact that blood smears may show AFB even in patients belonging to types classifiable as BT-BB in the Ridley Jopling scale (a child aged 3½ years showed this feature) emphasizes the importance of investigations to assess thoroughly the extent of bacillation in leprosy patients.

[The technique for the preparation of smears from heparinized blood is described.]

7. PATTYN, S. R., DOCKX, P., JACOB, W., ROLLIER, R. & ROLLIER, M. T. ***Mycobacterium leprae* in human skeletal muscle.** *Ann. Soc. Belg. Méd. Trop.*, 1975, v. 55, No. 6, 643-646.

Leprosy bacilli were found in 24 out of 31 muscle biopsies from treated lepromatous patients. Bacilli were localized within macrophages and endothelial cells of the interstitial connective tissue, none were found inside muscle cells. This may be the result of treatment. Morphological intact bacilli were not observed. The widespread occurrence of leprosy bacilli in the human body is in accordance with the concept that leprosy is a generalized infectious disease.

8. PADMA, M. N. & DESIKAN, K. V. **Bacillaemia in leprosy.** *Indian J. Med. Res.*, 1975, v. 63, No. 6, 888-892.

In this careful and well-documented study, the authors found alcohol-acid-fast bacilli in the venous blood of 77 out of 114 patients with lepromatous leprosy. Stringent precautions were taken to avoid contamination of the blood sample by bacilli present in the dermis overlying the punctured vein from which blood was taken. The buffy coat (obtained after centrifugation at 1500 rev/min) was spread on a clean new microscope slide and stained by Ziehl-Neelsen's technique. Of the 77 cases in which bacilli were found, in 67 they were present within leucocytes, 62 of them being in monocytes; in 29 of these, they were also present extracellularly. Solid rods (morphologically normal, and presumably viable bacilli) were found in 19 cases.

Although bacilli were present on average in only 1 field in every 500 examined, the total bacillary load per ml of plasma might be as high as over 40,000.

These findings [which incidentally confirm the routine examinations in some laboratories 40 years ago] are discussed in the light of the well-known observation that endothelial cells engorged with viable leprosy bacilli are often found lining the blood vessels in sections of skin from patients with lepromatous leprosy. Further studies are necessary to determine whether the bacteraemia is intermittent or constant, whether it is to be correlated with clinical activity or acute exacerbation, and whether with more delicate staining techniques bacilli could be demonstrated with greater ease and in patients with non-lepromatous leprosy.

S. G. Browne

9. BALENTINE, J. D., CHANG, S. C. & ISSAR, S. L. Infection of armadillos with *Mycobacterium leprae*. Ultrastructural studies of peripheral nerve. *Arch. Path. Lab. Med.*, 1976, v. 100, No. 4, 175-181.

Peripheral nerves of armadillos were studied 16 to 30 months after intradermal or intravenous inoculation with *Mycobacterium leprae*. Numerous bacilli were found within macrophages, Schwann cells, and perineural cells; endothelial cells, pericytes and fibroblasts were involved as well. The bacilli were characteristically contained in membrane-limited vacuoles that were interpreted as being phagosomes. Some of the phagosomes contained granular, membranous, and vesicular debris considered to be bacillary degradation products, suggesting that lysosomal activity was present within the phagosomes. Multivesicular bodies, a few of which contained bacilli, were abundant in macrophages and perineural cells. An unusual proliferation of irregular tubulovesicular profiles was noted, especially in Schwann and perineural cell cytoplasm, surrounding and within phagosomes containing bacilli. The pattern of cellular involvement of neural structures with *M. leprae* was similar to that observed in lepromatous leprosy neuritis in humans.

10. MATSUO, E. & SKINSNES, O. K. Specific direct fluorescent antibody identification of *Mycobacterium leprae*. *Int. J. Lepr.*, 1975, v. 43, No. 3, 204-209.

*In vitro* cultivation of *M. leprae* requires a rapid, specific identification procedure for monitoring the cultures. A method utilizing direct FITC-coupled lepromatous, specific serum globulin is described in detail with suggestions for improvement. After various purification and adsorption procedures, notably against human liver powder and *M. tuberculosis*, a fluorescent serum preparation is obtained which specifically reacts with *M. leprae* and not with other mycobacteria.

## 2. BIOCHEMISTRY, PATHOLOGY, IMMUNOLOGY

11. CONVIT, J., PINARDI, M. E., AVILA, J. L. & ARANZAZU, N. Specificity of the 48-hour reaction to Mitsuda antigen. Use of a soluble antigen from human and armadillo lepromin. *Bull. Wld Hlth Org.*, 1975, v. 52, No. 2, 187-191.

Two antigens were tested and compared in relation to the 48-h Fernandez reaction. They were obtained from standard human and from standard armadillo lepromin. All the tests were negative in patients with lepromatous leprosy and highly positive in those with tuberculoid leprosy and in lepromin-positive contacts. There was total agreement in all tests done with the two types of antigen. The antigen component has the following basic properties: it precipitates with 80% saturated ammonium sulfate; it is not destroyed by autoclaving or by treatment with 0.4% phenol; it is non-dialysable; and it is destroyed by treatment with trypsin.

12. CONVIT, J. *et al.* Tests with three antigens in leprosy-endemic and non-endemic areas. *Bull. Wld Hlth Org.*, 1975, v. 52, No. 2, 193-198.

A study comparing the 48-h and 30-day reactions produced by three antigens was made in areas of low and high leprosy endemicity in Venezuela and in areas of Chile, a non-endemic country. The antigens used for the intradermal tests were standard Mitsuda antigen, supernatant from standard Mitsuda antigen, and PPD. The results indicate that there is no difference in the Mitsuda reaction of persons living in areas of high or low endemicity, but they show a statistically significant difference between the reactions in persons who live in endemic areas and those of persons living in a country where the disease has not been described. The

difference in the Fernandez reaction obtained with the supernatant was not statistically significant between the two population groups in the endemic country, but was highly significant when comparing the endemic and the non-endemic countries.

13. LIM, S. D., JACOBSON, R. R., PARK, B. H. & GOOD, R. A. **Leprosy XII. Quantitative analysis of thymus-derived lymphocyte response to phytohemagglutinin in leprosy.** *Int. J. Lepr.*, 1975, v. 43, No. 2, 95-100.

The immune status of various leprosy patients was evaluated by using a micromethod to evaluate lymphocyte responses to phytohemagglutinin (PHA). In our study, whole blood was used and the degree of response to PHA stimulation was expressed in terms of unit volume of blood. A markedly decreased response to PHA stimulation was noted in patients with active lepromatous leprosy. Patients with active lepromatous leprosy who have been proved drug (DDS) resistant showed less response than did those of drug sensitive patients with active lepromatous disease, while the patients with active lepromatous leprosy complicated by *erythema nodosum leprosum* (ENL) showed higher response than did those of patients with no complicated ENL.

Comparing the results obtained to those obtained using other methods for T cell analysis indicates that these results reflect the number of T lymphocytes in the leprosy patient. Thus, this simple method is of value in assaying the presence and responses of T lymphocytes in the leprosy patient.

[For Pt XI, see *Trop. Dis. Bull.*, 1975, v. 72, abstr. 1663.]

14. SHER, R., HOLM, G., KOK, S. H., KOORNHOF, H. J. & GLOVER, A. T. and CR<sup>+</sup> **lymphocyte profile in leprosy and the effect of treatment.** *Infection & Immunity*, 1976, v. 13, No. 1, 31-35.

Thymus-derived lymphocytes (T lymphocytes) and complement receptor-bearing lymphocytes (CR<sup>+</sup> lymphocytes) were estimated by using erythrocyte rosettes and erythrocyte-antibody-complement rosettes as markers in untreated lepromatous and untreated tuberculoid patients and in healthy controls. Treated lepromatous cases were also investigated. Ten cases of untreated lepromatous patients were reassessed 6 months or more after therapy commenced. A significant decrease in both percentages and absolute numbers of CR<sup>+</sup> cells in the untreated lepromatous leprosy subjects was observed. This decrease showed a return to normal levels after treatment. The percentage of T cells in the untreated lepromatous cases was normal; however, the absolute numbers of T cells and the total lymphocyte count showed a significant decrease. After therapy, the T cell population was unchanged but the total number of lymphocytes increased significantly with treatment. The absolute number of T and CR<sup>+</sup> cells was significantly less in the untreated than in the treated lepromatous patients.

15. REA, T. H., GOTTLIEB, B. & LEVAN, N. E. **Apparently normal skin in lepromatous leprosy. Histopathological findings.** *Arch. Derm.*, 1975, v. 111, No. 12, 1571-1574.

Biopsy specimens of apparently uninvolved skin from 34 patients with lepromatous leprosy were studied histologically. Bacilli were found in 30 of 31 specimens from clinically polar or near-polar lepromatous patients but not in the 3 from nonpolar patients. A predominantly perivascular distribution of infiltrate and bacilli is consistent with the hematogenous spread of infection. Subclinical, diffuse lepromatous leprosy is found in patients with nodular lesions and may precede the development of nodules. Study of apparently uninvolved skin may be helpful in classifying patients, in interpreting immunologic responses, and in elucidating the natural history of the illness.

16. HALDAR, B. & DUTTA, A. K. Cutaneous vascular reactivity in tuberculoid leprosy lesion. *Lepr. India*, 1975, v. 47, No. 4, 307-315.

In order to study the nervous and non-nervous cutaneous vascular responses in tuberculoid lesions of leprosy under chemical, mechanical and thermal stimuli, the following experimental studies were performed in 38 cases with control study in each:

- (i) Adrenaline induced blanch reaction and periblanche erythema.
- (ii) Focal bleeding time.
- (iii) Surface temperature variations and adjustments following local application of cold.

In the lesions the results showed less prolonged blanch reaction and ill-developed periblanche-erythema, relatively prolonged focal bleeding time; slightly lesser degree of initial surface temperature, higher degree of declination in surface temperature following cold application and higher level of rise following heat application. Hunting type of reaction after both heat and cold applications was observed in control and test sites almost equally.

The collective results testify the phenomenon of inhibited nerve tonus in leprosy lesions consequent to organic affection of sympathetic fibres resulting in a vascular atonia.

17. DÍAZ ALMEIDA, J. G., TORRES, G. & ABREU, A. Deficiencia de glucosa 6-fosfato-deshidrogenasa en el enfermo de lepra. Informe preliminar. [Glucose-6-phosphate dehydrogenase deficiency in leprosy. A preliminary report.] *Revta Cub. Med.*, 1975, v. 14, No. 5, 687-691.

The English summary appended to the paper is as follows:

For the first time in Cuba a preliminary study on glucose 6-phosphate dehydrogenase (G6PD) deficiency using a modification of the Beutler's method (Kapa's system) in patients from Havana Leprosarium is made for determining the relation between G6PD deficiency and a lower defensive capacity of the organism against *M. leprae*. An enzyme deficiency only in patients with the lepromatous form and in those with backgrounds of repeated acute reactions was found.

18. MEHTA, L., SHETTY, V. & ANTIA, N. H. Study of early nerve lesions in mice infected with *M. leprae*. *Lepr. India*, 1976, v. 48, No. 1, 31-35.

The present study is of quantitative histology in immunologically intact mice inoculated with *M. leprae*. Total 12 sciatic nerves are studied. The fibres are grouped as large, medium and small sized fibres. Initially there is loss of small sized fibres. At later stages there is involvement of all sized fibres and ultimately Wallerian type of degeneration sets in. The process of regeneration is more active than that of human leprosy of tuberculoid type. This study adds a new dimension in understanding the pathogenesis of leprosy.

[This paper is illustrated with 5 electron micrographs on plates.]

19. BEDI, B. M. S., HARRIS, E. B., NARAYANAN, E. & KIRCHHEIMER, W. F. Delayed hypersensitivity tests with *Mycobacterium leprae* purified protein derivative. *Lepr. India*, 1976, v. 48, No. 1, 8-18.

Skin tests were conducted on 3 lepromatous, 3 dimorphous and 6 tuberculoid leprosy patients and 3 others not suffering from leprosy with lepromin, purified protein derivative from *M. leprae* of armadillo origin and tuberculin. Results show that a delayed hypersensitivity reaction could be produced with PPD in 72 hours on all Mitsuda positive cases, with one anomalous exception, without cross reaction to tuberculin. The results were promising from the point of view of substituting lepromin with PPD in usual tests.

20. CHEN, T. S. N., DRUTZ, D. J. & WHELAN, G. E. **Hepatic granulomas in leprosy: their relation to bacteremia.** *Arch. Path. Lab. Med.*, 1976, v. 100, No. 4, 182-185.

A clinicopathologic study of liver disease was conducted on 28 patients with leprosy who lived in Taiwan. None of the patients exhibited symptoms or signs of liver disease. Hepatic granulomas were found in 21 patients. Histologically, the infiltrates were epithelioid, foam cell, and histiocytic in type. Hepatic dysfunction was absent, except for mild sulfobromophthalein elevations in the severely infected cases. Hepatic granulomas correlated with the cutaneous reactions in lepromatous leprosy, but the association was poor for other stages of disease. Hepatic involvement varied with the severity of cutaneous infection and with the frequency and intensity of bacteremia. An estimated 1000 to 10,000 acid-fast bacilli/ml of blood was required to generate the hepatic infiltrates.

21. SAHA, K., DUTTA, R. N. & MITTAL, M. M. **Immunologic aspects of leprosy as related to leucocytic isoantibodies and platelet aggregating factors.** *Int. J. Lepr.*, 1975, v. 43, No. 3, 239-248.

The incidences of various iso- and autoantibodies in a random population of 112 unselected leprosy patients is presented. Low titers of leucocytic isoantibodies and platelet aggregating factor were detected in the sera of a variable number of such patients. The leucoisoagglutinins were found in 8% of the sera of tuberculoid as well as lepromatous leprosy patients, whereas the leucocytotoxins were detected in a larger percentage of the lepromatous (40%) as well as tuberculoid (28%) cases. The platelet aggregating factors (PAF) were positive in 51.2% and 45% of lepromatous and tuberculoid cases respectively. Of the 21 positive sera for PAF, the antiplatelet factor by antihuman globulin consumption test could be demonstrated only in 66.6% and 50% of lepromatous and tuberculoid sera respectively. To study the frequencies of these newly detected antibodies or antibody-like factor and to compare their occurrences with other well-documented autoantibodies present in the sera of leprosy patients: cryoglobulins, antinucleoprotein antibody and thyroglobulin autprecipitin were also studied in the sera of the same population of leprosy patients. It has been observed that the simultaneous occurrence of all these auto- and isoantibodies in the serum of one patient is a rare phenomenon. Leucocytic and platelet counts of these patients having antibodies against leucocytes and platelets were found to be within normal limits. Accordingly, it is suggested that the low levels of antileucocyte antibody and antiplatelet factor are probably harmless to the hosts. On the other hand, it is postulated that these antibodies may act as enhancing factors by being specifically adsorbed on the lymphoid cells, thus rendering them unresponsive to mitogenic stimulus *in vitro*. From these studies it seems that leprosy, especially the lepromatous type, is associated with some of the serological features suggestive of an autoimmune aberration.

22. LOUIE, J. S. & GLOVSKY, M. **Complement determinations in the synovial fluid and serum of a patient with erythema nodosum leprosum.** *Int. J. Lepr.*, 1975, v. 43, No. 3, 252-255.

Simultaneous serum and synovial fluid CH50, C1, C4, C2, C1 esterase inhibitor and C3 protein were determined in a patient with acute erythema nodosum leprosum. The pattern of synovial fluid complement activity coupled with the demonstration of multiple lepra bacilli free and within histocytes is more consistent with an infectious than an immune complex induced synovitis.

23. SAMUEL, I., SAMUEL, D. R. & GODAL, T. Hepatitis associated antigen (HAA) in leprosy. *Ethiop. Med. J.*, 1974, v. 12, No. 4, 175-178.

One hundred and forty leprosy patients selected from the outpatient department of ALERT, Addis Ababa, were tested for hepatitis-associated antigen in their blood. Eleven or 8% of these patients were positive for HAA. The prevalence of HAA in leprosy patients was not significantly higher than in the normal population. Our studies did not show any increase in the prevalence of HAA in lepromatous cases as compared to tuberculoid cases.

### 3. CLINICAL

24. REA, T. H. & LEVAN, N. E. Erythema nodosum leprosum in a general hospital. *Arch. Derm.*, 1975, v. 111, No. 12, 1575-1580.

This is a study of 32 patients in Los Angeles, California, suffering from lepromatous leprosy complicated by erythema nodosum leprosum (ENL) reaction. There were 17 men and 15 women in the series, their ages ranging from 18 to 72 years, and 22 of these patients first presented with ENL reaction although they had never received any anti-leprosy treatment. In 5 women the initial attack of ENL occurred during pregnancy.

The authors describe the clinical, laboratory and histological findings, and discuss the possible mechanisms involved. They stress that their experience is contrary to the generally held opinion that this type of reaction usually complicates anti-leprosy therapy, and suggest that it should be considered to be a manifestation of leprosy rather than a complication of its treatment.

*W. H. Jopling*

25. QUAGLIATO, R., BECHELLI, L. M., ALMEIDA, J. O. & ARANTES, M. A. A. Bacteriological status (point prevalence) of lepromatous outpatients under sulphone treatment. *Bull. Wld Hlth Org.*, 1975, v. 52, No. 1, 57-62.

This is a study of 337 patients with lepromatous leprosy who had been under dapsone therapy as outpatients for 1-26 years in São Paulo, Brazil. 167 (50%) showed bacteriological positivity of skin smears when the slides were examined by a paramedical technician, who spent 10 min on each slide, but the rate was 99% when each slide was examined for 30-60 min by a bacteriologist. The authors conclude that, in mass campaigns, bacteriological negativity should be checked by a well-trained bacteriologist and the smears should be made by an experienced leprologist, before lepromatous patients are released from supervision.

[A more practical conclusion would be that lepromatous patients should be treated for life.]

*W. H. Jopling*

26. TIN SHWE, MYA THEIN & SOE MINT. Prevalence of pulmonary tuberculosis in patients with leprosy. *Burma Med. J.*, 1975, v. 21, 39-44.

The authors quote figures showing the high incidence of pulmonary tuberculosis among leprosy patients being treated in leprosaria in various parts of the world, figures which suggest that persons suffering from leprosy have an increased susceptibility to tuberculosis. This investigation, designed to establish if there is any justification for such a hypothesis, was confined to leprosy outpatients attending clinics at Rangoon General Hospital, and 603 patients aged between 20 and 40 years were studied (301 tuberculoid and 302 lepromatous). Seven patients with radiological evidence of pulmonary tuberculosis were found in the tuberculoid



group (2.3%) and 8 in the lepromatous group (2.6%), figures which compare favourably with those from Burma as a whole among adults of similar age-group (2.6-3.6%). Two important conclusions can be drawn from this study: firstly, that figures giving the incidence of pulmonary tuberculosis among in-patients in leprosia bear no relation to the situation in that particular region or the country as a whole; secondly, that patients suffering from the lepromatous type of leprosy are no more susceptible to tuberculosis than are those suffering from the tuberculoid type.

W. H. Jopling

#### 4. THERAPY

27. GELBER, R. H. & REES, R. J. W. Dapsone metabolism in patients with dapsone-resistant leprosy. *Am. J. Trop. Med. Hyg.*, 1975, v. 24, No. 6, 963-967.

Acetylation of dapsone (DDS) and sulfamethazine (SMZ), and plasma clearance of DDS were studied in Malaysian Chinese with lepromatous leprosy including 40 DDS-resistant and 44 non-resistant patients. Neither a patient's acetylation characteristics (DDS or SMZ), nor his plasma clearance rate, appeared to have predisposed him to the development of DDS resistance. A potentially important drug interaction between rifampin and DDS was discovered. After ingestion of rifampin for a minimum of 2 weeks, the plasma clearance of DDS was increased and the relative amount of the acetylated DDS was decreased. The implications of these results for the treatment of lepromatous leprosy are discussed.

28. CHAUDHRY, S. B. R. & DESIKAN, K. V. Sulphone-resistance in leprosy: a report of three cases. *Lepr. India*, 1975, v. 47, No. 4, 283-290.

The experimental transmission of leprosy to the foot-pads of mice has provided a very useful technique to demonstrate the occurrence of sulphone-resistant strains of *M. leprae*. Although this method is at present the most satisfactory laboratory confirmatory test, it is not practicable to apply it to screen a very large number of cases of leprosy under sulphone therapy today. A clinical detection of sulphone-resistance is therefore very essential. Three cases of lepromatous leprosy detected clinically to be sulphone-resistant and proved subsequently by the mouse foot-pad model are reported.

[A report from Chingleput, Tamil Nadu, India.]

29. LEVY, L. & PETERS, J. H. Susceptibility of *Mycobacterium leprae* to dapsone as a determinant of patient response to acedapsone. *Antimicrob. Agents Chemother.*, 1976, v. 9, No. 1, 102-112.

In the course of a clinical trial of acedapsone therapy in 17 patients with lepromatous leprosy, the rate of response to therapy was measured by inoculation of mice with *Mycobacterium leprae* recovered from biopsy specimens of skin lesions obtained before treatment and at intervals of 4, 12, and 24 weeks after institution of treatment. The susceptibility of each isolate of *M. leprae* to dapsone (4,4'-diaminodiphenylsulfone [DDS]) was measured by passaging organisms that had multiplied in mice to new groups of untreated mice and to mice treated with DDS incorporated in the mouse chow in concentrations of  $10^{-5}$ ,  $3 \times 10^{-5}$ , and  $10^{-4}$  g/100 ml. The rate of response to acedapsone therapy and the susceptibility of patient strains of *M. leprae* to DDS varied widely among patients. All isolates were inhibited from multiplication by treatment of mice with  $10^{-4}$  g of DDS per 100 ml; all but two isolates were susceptible to  $3 \times 10^{-5}$  g of DDS per 100 ml; and 17 of 36 isolates, representing nine patient strains, were susceptible to  $10^{-5}$  g of DDS per 100 ml. Plasma levels of DDS measured in the

mice administered these diets show that the minimal inhibitory concentration of DDS for *M. leprae* isolated from untreated patients is about 3 ng/ml. No relationship could be demonstrated between DDS susceptibility of pretreatment isolates of *M. leprae* and the rate at which patients responded to acedapsone therapy. Neither acedapsone treatment of patients nor DDS treatment of mice appeared to select genotypically more resistant *M. leprae*.

## 5. EPIDEMIOLOGY AND CONTROL

30. KYAW LWIN & ZUIDERHOEK, B. Case detection rates for Central Burma (1962-1972). *Int. J. Lepr.*, 1975, v. 43, No. 2, 125-128.

A short description of the leprosy control program in Burma is given and the decrease of the case detection rates during the period 1962-1972 are presented to show the effects of control measures in the program emphasizing the importance of early case detection through annual examination of household contacts and school children, regular treatment and health education.

31. JARAMILLO, A. O. & DE LA CRUZ, M. R. Le lepra en Costa Rica. *Acta Méd. Costarric.*, 1975, v. 18, No. 3, 151-207.

The first person with leprosy recorded in Costa Rica was the child of a Spanish family in about 1734. By 1883 there were 32 leprosy patients in a lazarette. Sulphonotherapy was introduced in 1945 and the first cure was recorded in 1947. The Department for the Control of Leprosy was created in 1948. Active prophylaxis was initiated in 1952 with the compilation of a register of contacts. From 1954, cutaneous lymph was collected for diagnosis from persons living with patients. In 1962 a specialist was appointed to conduct a dermatoneurological examination of all contacts. A "new programme for the control of leprosy in Costa Rica" was created in 1974 which prohibited the internment of patients in the leprosy sanatorium and decreed that they should be treated in general hospitals. A rehabilitation programme was also initiated. By 1974 there were 518 registered cases, and their geographical distribution is recorded, but it is estimated that there are probably some 1300 cases. The spread of the disease is to be controlled by dermatological examination of all suspects and groups of persons at risk. Persons living with a patient must be examined dermatoneurologically once a year for 5 years; at present, 3282 contacts are under observation. Chemoprophylaxis is appropriate for juveniles living in close contact with a patient in the lepromatous or dimorphic stage. Leprosy patients should generally be treated in outpatient clinics and should be examined dermatoneurologically and bacteriologically twice a year in the case of those with lepromatous or dimorphic lesions and once a year in tuberculoid and indeterminate cases.

*Ann Grant*

32. LECHAT, M. F., MISSON, J. Y., VELLUT, C. M., MISSON, C. B. & BOUCKAERT, A. Un modèle épidémiométrique de la lèpre. [An epidemiometric model of leprosy.] *Bull. Wld Hlth Org.*, 1974, v. 51, No. 4, 361-373. English summary.

This valuable paper, which breaks new ground, should be consulted in the original by all concerned with the epidemiology and control of leprosy. Taking as their bases a mass of

observations collected over 16 years in the Belgian Leprosy Centre at Polambakkam, India, concerning 35,262 leprosy patients, the authors have elaborated a tentative epidemiometric model that should be tried out in other situations.

The model takes cognizance of 10 different states of leprosy infection, which correspond to the different stages through which any individual is presumed to pass, from "susceptible" and "latent" to "inactive" and "no longer taking treatment". Certain assumptions are made, some of which are open to question and need clarification, e.g. every individual is born susceptible to leprosy infection and may contract the disease if exposed to effective contact; any person with active leprosy may serve as a source of infection; tuberculoid leprosy may pass into the lepromatous form, through an intermediate stage; transition from active to inactive is a clinically based decision, although infectivity is assumed; the risk of relapse is identical, whether patients whose leprosy is quiescent take treatment or not; the latent form always develops into active leprosy, which does not regress in the absence of treatment.

A detailed analysis of the Polambakkam statistics allows the authors to suggest a series of mathematically expressed equations for several parameters, which have been used in a computerized simulation of leprosy prevalence and incidence rates in a variety of hypothetical and actual situations.

Preliminary results run closely parallel in certain respects to accepted epidemiological findings dating back some years, such as the observations that patients with lepromatous leprosy are 4 times as contagious within the household as those with tuberculoid leprosy, that infectivity diminishes rapidly with anti-leprosy treatment, that (because of their numbers) patients with tuberculoid leprosy play a major part in the persistence of the leprosy endemic. The model indicates that, whereas the latent period of tuberculoid leprosy is about 4 years, that of lepromatous leprosy is but 2.2 years. After 10 years of treatment, the chances of a patient with lepromatous leprosy becoming "cured" are practically nil.

Some tentative conclusions are of immediate applicability. A reduction in the rate of default would show a greater effect on the endemic than segregation of patients with lepromatous leprosy. A vaccine that would prevent the development of lepromatous leprosy would show the greatest beneficial results. Intensification of case-finding activities and the placing under effective treatment as soon as diagnosed of all persons suffering from leprosy, and especially those with lepromatous leprosy, are desirable goals, if not immediately achievable throughout the world.

*S. G. Browne*

33. RAO, P. S. S., KARAT, A. B. A., KALIAPERUMAL, V. G. & KARAT, S. **Transmission of leprosy within households.** *Int. J. Lepr.*, 1975, v. 43, No. 1, 45-54.

The wealth of statistical data available in the records accumulated in the Gudiyatham Taluk (Tamil Nadu, India) leprosy programme is exemplified by this analysis. During the years 1962 to 1970, in a population of about 400,000, over 97% of the 23,285 contacts in 5088 families having a leprosy patient were examined clinically. Against an annual incidence of leprosy of the order of 0.8 per 1000 patient-years in the general population, the incidence among household contacts was 6.8 per 1000 patient-years. The rates for males and females, when analysed for each of the major types of leprosy and expressed as total sex incidence, showed no appreciable differences. Where the index case in the household suffered from a multibacillary form of leprosy, the secondary attack rate was significantly higher.

The most vulnerable age-groups were found to be 5-14 years for boys, and 5-9 years for girls, the actual clinical manifestations appearing after a variably long latent period. When there was more than one index case in the family, the attack rate doubled. When the index case was of a bacilliferous type of leprosy, there was a higher proportion of such types among the secondary cases [a possibly fortuitous finding that does not imply strain differences].

*S. G. Browne*

34. RASI, E., CASTELLAZZI, Z., GARCIA, L., QUEVEDO, L. & CONVIT, J. Evaluation of "chemical isolation" in 1168 leprosy patients' homes. *Int. J. Lepr.*, 1975, v. 43, No. 2, 101-105.

"Chemical isolation" (treatment of open cases as a measure of control for transmission between contacts) is evaluated by a retrospective study of 7232 household contacts of 1168 leprosy patient homes. Contacts comparable in age and type of exposure were arranged in subgroups according to whether they were born before (Group A) or born after (Group B) beginning treatment of the index cases had begun. Additionally, the whole group of contacts, both of open (LL and BB) and close (TT and I) cases were evaluated.

Among comparable contacts of LL and BB cases, the infection rate in the contacts before initiation of treatment is higher than in that of contacts after initiation of treatment. The protection afforded by the treatment to the exposed group (Group B) is on the order of 66%.

The morbidity occurring in the group born after the initiation of index case treatment apparently results from partial persistence of infectiousness of the case under treatment.

## 6. SOCIOLOGY AND REHABILITATION

34. ROTBERG, A. The ten enemies of prevention of hanseniasis are related to "Leprosy". A "Psycho-social-somatic phenomenon". Reprinted from *Leprologia*, 1974, v. 19, No. 2, 281-285.

*Leprosy* is not a disease like any other, but a chain of phantasies, superstitions, stigma, sensationalism, ignorance, fear, rejection and infamous terminology—around a core of signs and symptoms of the somatic disease. One of the consequences is that we are still *case finding* instead of seeing patients and contacts *finding us*. The ten enemies of prevention are: (1) Latent segregationism; (2) hesitant integrationism; (3) the infamous pejorative *leprosy*; (4) sensationalism; (5) misguided charity; (6) psycho-social amateurism; (7) non-attentive education; (8) low salaries and lack of personnel; (9) obsolete legislation; (10) deficient teaching. . . .

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