Lep. Rev. (1967) **38**, 2, 120-127

Abstracts

1. **Experimental Studies in Leprosy. Recent Applications of Experimental Human Leprosy in the Mouse Foot Pad,** by R. J. W. Rees. *Leprosy in India*, 1965, 3A, July Supplement.

We set out several years ago to see whether the viability of leprosy bacilli could be determined indirectly by morphological appearances. In our early studies we used *Myco. lepraemurium* as our model because a final check could be made on the viability (measured as infectivity) by putting the bacilli back into mice or rats and seeing whether they produced disease. The results of those studies showed conclusively that living and dead *Myco. lepraemurium* could be identified by their different morphological appearances and that these appearances were seen in bacilli stained by the classical Ziehl-Neelsen method. All bacilli that showed irregular staining were incapable of producing disease in animals and therefore were considered dead. We then extended our studies to *Myco. leprae* where we were able to show identical morphological differences. Therefore it was reasonable to conclude, since the morphological changes were common to any type of dead bacteria, that these same methods could be used for distinguishing dead and alive *Myco. leprae*. At that time we could not put these observations to direct test with *Myco. leprae* because the organism could neither be cultured nor transmitted to experimental animals. Now that there is available the mouse foot-pad infection it should be possible to carry out the same type of experiments we used for *Myco. lepraemurium*. One approach to this type of study is already in hand in our own laboratories. A series of experiments have been set up inoculating the mouse foot-pad with bacilli from patients who have received 12 or more months' treatment with DDS and where there are very high proportions of 'degenerate', irregularly staining acid-fast bacilli. Preliminary results indicate that in none of these mice followed now for periods up to 15 months has any infection been produced, whereas bacilli from previously untreated patients would have produced active disease and at least 100 fold increase in the number of bacilli within a period of 6-8 months. Therefore, we already have strong evidence to suggest that bacilli coming from these treated patients have very reduced viability and this is consistent with the morphological appearances of these organisms. Shepard and McRae have also analysed their own data in an attempt to correlate infectivity in the mouse foot-pad with the morphological appearance of *Myco. leprae*, and their results show conclusively that there is a complete correlation proving that only solidly stained bacilli are infective (viable).

With these important results it should be possible to test the infectivity of nasal and ulcer secretions containing *Myco. leprae* under various 'natural' conditions in order to determine the importance of such secretions in the spread of leprosy.

(*From the author's summary.*)

2. **75 years of Organized Measures for Leprosy Control in Estonia,** by E. Roigas and R. Uetoa. *J. Dermat. & Venerol.*, Moscow, 1966, Oct.

Some data concerning the history of leprosy in Estonia since 1222 are presented. The foundation of leprosaria by the 'Society for Control of Leprosy in Livland' in 1891 must be considered as the first organized measure for control of leprosy in Estonia. Success achieved by the present time is described.

The following 8 abstracts are reprinted, with permission, from *Trop. Dis. Bull.*, 1966, **63**, 11 :

3. **White Spots in Biblical Times. A Background for the Dermatologist for Participation in Discussions of Current Revisions of the Bible,** by L. Goldman, R. S. Moraites and K. W. Kitzmiller. *Arch. Dermat.*, 1966, June, **93**, 6, 744-54, 7 figs. (12 refs.).

'Discussions of various religions in current revisions of the Bible should be of interest to dermatologists, for these discussions include reviews of the biblical concept of leprosy. Unfortunately, terms now suggested as substitutes for "leprosy", often considered in the Bible as a moral sin, include "affections of the skin" and even "psoriasis". The background of this ancient controversy is presented as regards the significance of white spots, the influences of ancient Greek medicine, current plans of some religions, and recommendations.'

4. **A Comparative Study of the Complementary Activity of Serum in the Polar Forms of Leprosy and in the Leprosy Reaction,** by M. Paca de Azevedo and P. Homen de Melo. *Inter. J. Lepr.*, Wash., 1966, Jan.-Mar., **34**, 1, 34-8, 1 fig.

'The authors studied complementary serum activity in 88 leprosy patients, divided into three groups: GroupT, 33 tuberculoid cases; Group L, 37 lepromatous cases; and Group R, 18 cases in lepra reaction (erythema nodosum and multiform types). The titration technic was that of Maltaner and Maltaner as described by Almeida, and the designations used for component and angular inclination were those of von Krogh. The average of complement unit (K) and of angular inclination (1/n) were compared statistically, with the following results:

'1. The average values of Groups T and L did not present significant differences.
'2. The average values of Group R presented differences that were significant in relation to the other two groups studied.
'3. The complementary activity in Group R was clearly decreased.
'4. It is probable that this decreased complementary activity is related to the autoantigen/autoantibody complement-fixing complexes found in

circulating blood. Their appearance may be explained by an immunologic phenomenon peculiar to lepromatous patients in a reactional stage.'

5. **The Value of Nasal Smears in Lepromatous Leprosy,** by S. G. Browne. *Inter. J. Lepr.*, Wash., 1966, Jan.-Mar., **34**, 1, 23-6.

This paper reports on the analysis of the results of the bacterioscopic examination of material obtained from the nasal mucosa in 100 patients suffering from lepromatous leprosy admitted to the Research Unit, Uzuakoli Leprosarium, Eastern Nigeria. In the routine procedure of obtaining the bacterial material, a Thudicum's speculum was inserted well into the nostril in such a way as to display the nasal septum, and then a swab dipped in spirit passed gently over the mucosa to remove excess mucus. Then, with a blunt spud, the septal mucosa was stroked firmly under direct vision and the material thus obtained was placed on a microscope slide and stained. With data obtained questions were proposed and answered. (1) Can *Mycobacterium leprae* be demonstrated in nasal smears before they appear elsewhere? *Answer:* in no patient in this series was the nasal mucosa the only site to show bacilli, and it is apparently very rare for the nasal mucosa to be the site of initial lesions. (2) Is there any possibility of confusing acid-fast contaminants with *Myco. leprae*? *Answer:* this theoretical objection carries little weight in practice. (3) Do nasal smears reflect the bacterial state in the skin and ear lobes? *Answer:* while examination of nasal smears of patients with lepromatous leprosy in Eastern Nigeria will not help materially in making or confirming the diagnosis of lepromatous leprosy, in about half the patients it provides additional information, for both B.I. and M.I. are higher than those from smears from other sites. (4) Is there additional information from the contralateral septal mucosa? *Answer:* nothing significant. (5) Does the nasal mucosa contain 'solid rods' after their disappearance from the skin and ear lobes? *Answer:* in about half the patients in whom definite differences existed the nasal mucosa harboured 'solid rods' longer than elsewhere. (6) Does the nasal mucosa contain fragmented bacilli after their disappearance from the skin and ear lobes? *Answer:* there is no marked difference. (7) Is there any correlation between the absolute height of the B.I. when the patient is first examined and the proportion of 'solid rods' in the nasal mucosa and at the other sites? *Answer:* no. (8) When morphologically normal *Myco. leprae* reappear after an interval, or when degenerate forms reappear, is the nasal mucosa predominantly involved? *Answer:* there is evidence that the nasal mucosa may be involved precociously when normal or degenerate *Myco. leprae* reappear for a shorter or longer period after they have disappeared for some months from all sites smeared.

Globi are frequently more numerous in the nasal mucosa and persist longer than elsewhere.

The author's bacteriological study is of great interest and this paper merits close study.

J. R. Innes.

6. **Lepra Reaction. Its Relation with Fragmentation of *Mycobacterium leprae* under Sulfone Therapy,** by A. Saul and N. Segura. *Inter. J. Lepr.*, Wash., 1966, Jan.-Mar., **34**, 1, 17-22, 4 figs. (19 refs.).

Some immunological hypotheses relating to lepra reaction are reviewed. The authors set out to investigate the effect of DDS on the fragmentation of leprosy bacilli, and the influence of such fragmentation on the occureence of reactions. For these purposes a retrospective survey was made of the records of 429 patients in Mexico with lepromatous leprosy treated with DDS and a special study was made of 10 new patients who had not received treatment.

Lepra reaction occurred in 237 of the 429 patients. Fragmentation of bacilli was noted in 74% of those who reacted and in 18% of non-reactors. Fragmentation of bacilli was seen before treatment with DDS had begun in 45% of the patients, and 32% had some reaction in the pre-treatment stage. DDS did not seem to be the principal cause of reaction or the sole cause of fragmentation. Of the 10 patients who received special study, 9 had already had lepra reaction before treatment commenced. There was no close correlation between subsequent acute attacks and the appearance of fragmentation, and no cause and effect relationship could be detected between the two.

(Reactions before treatment in 9 out of 10 patients is an exceptionally high incidence. The abstracter's own study of this problem, which is quoted, was concerned with factors affecting the first onset of reaction. Subsequently there is great irregularity in the distribution of solid and fragmented bacilli due to reaction in some lesions and, probably, a recurrence of the infection in others.)

D. S. Ridley.

7. **A Trial of Thalidomide in Progressive Lepra Reactions,** by R. J. Cazort and Ye Kun Song. *Current Therap. Res.*, New York, 1966, June, **8**, 6, 299-311, 3 figs.

The authors describe progressive or recurrent lepra reaction as the most serious of the reactional states in lepromatous leprosy. It is commonly manifested by outbreaks of small subcutaneous nodules, pain in bones and nerves, leucocytosis, fever, insomnia, lethargy, and anorexia, and less frequently by iridocyclitis and orchitis. Various synthetic adrenal corticosteroids have proved to be effective suppressives of lepra reactions, but attempts to stop them result in acute exacerbations in the reactions.

Sheshkin (this *Bulletin*, 1965, v. 62, 1007) reported rapid subjective improvement with the use of thalidomide which was first synthesized by Kuntz *et al.* (*Arzneimittal-Forsch*, 1956, v. 6, 426) as a substitute for the barbiturates, and studies revealed that it possessed hypnotic action. Sheshkin made no mention of toxic effects in his first report, in which the drug was used for periods up to 4 weeks. However, in a subsequent paper he did list numerous toxic effects when thalidomide was used for periods up to 10 months.

The present authors give the results of a therapeutic trial on 24 patients suffering from reactional leprosy in Chiengmai Hospital and McKean Leprosy Hospital, Chiengmai, Thailand. The criteria of entry to the trial were a diagnosis of lepromatous leprosy, a diagnosis of recurrent lepra reaction, previous treatment with prednisolone for periods of at least one week and a period of one week or more since the last treatment with DDS.

Prednisone was discontinued in all but 4 patients, 2 days before thalidomide was commened. However, by this time the corticosteroid had been gradually reduced to half the original dose. In 4 patients no attempt had been made to reduce the dose, or to withdraw it completely. Thalidomide was given orally in tablet form, 3 tablets of 100 mgm. per day.

The authors report efficacy in the relief of severe lepra reactions. The subcutaneous nodules and associated erythema disappeared, pains in muscles, joints and nerves were considerably lessened or completely removed, body temperatures returned to normal, elevated white counts and sediment rates were lowered and general condition of the patients appeared much improved. There is a possibility of an immunosuppressive action by thalidomide in the lepra reactions. Three patients in 2 weeks of the therapy suffered acute exacerbations of the lepra reactions. At the end of the trial when thalidomide was withdrawn all patients had relapses. Thalidomide seemed to offer some protection against reactions induced by DDS. The results over the short period of 2 weeks support the claim of some beneficial effect in progressive lepra reactions. However the occurrence of relapses indicates that thalidomide alone and in the doses used is not continuously effective and the spectrum of untoward effects indicate that after its use for a short time it is not likely to interrupt permanently the cycle of recurrent or progressive lepra reactions.

J. R. Innes.

8. **A talidomida nos surtos agudos da lepra. (Eritema nodoso ou polimorfo.)** (Thalidomide in the Acute Crisis of Leprosy), by D. V. A. Opromolla, L. S. Lima and M. B. Marques. *Hosp.*, Rio de Janeiro, 1966, Apr., **69**, 4, 827-44, 5 figs. and 2 charts.

The authors have confirmed that thalidomide is effective in the control of reactions in leprosy and its continued administration prevents new attacks of reaction (this *Bulletin*, 1966, v. 63, 285).

The authors treated 43 patients who had lepra reaction in lepromatous leprosy, and a group of borderline patients, with thalidomide. The drug was administered in a dose of 100 mgm. daily, and then on alternate days. With the doses used no side effect was observed. When treatment was stopped 5 to 10 days later the nodules of lepra reaction and fever reappeared.

The authors think that thalidomide should be used because it offers a chance of instituting direct attack on the disease itself. This paper calls for careful study throughout.

J. R. Innes.

9. **Vaccination against Human Leprosy Bacillus Infections of Mice: Protection by BCG given during the Incubation Period,** by C. C, Shepard. *J. Immunology*, 1966, Feb., **96**, 2. 279-83, 1 fig. (12 refs.).

The author has already shown that BCG vaccination protects mice against footpad infections with *Mycobacterium leprae* (this *Bulletin*, 1965, v. 62, 880). To see whether vaccination during the incubation period of the experimental infection would provide protection, groups of mice were given 1 or 2 injections of BCG at intervals before or after challenge with *Myco. leprae.* Vaccination 1-2 months before challenge was found to give the expected degree of protection, immediately after challenge it gave no protection, but later on in the incubation period, during the logarithmic phase of growth, vaccination gave increasing protection up to the level attained in the pre-challenge period. By analogy BCG vaccination of human beings early or late during the incubation period would be expected to provide protection against leprosy.

D. S. Ridley.

10. **Further Studies on B.663 in Murine Leprosy. Absence of Resistance of *M. lepraemurium* to B.663 and Delay in Development of Resistance to Isoniazid,** by Y. T. Chang. *Inter. J. Lepr.* Wash., 1966 Jan.-Mar. **34**, 1, 1-6. 1, fig.

Isoniazid has been reported to enhance the action of B.663 (by itself an unusually effective drug) against *Mycobacterium lepraemurium.* A study was made of the influence of the combination on the development of resistance to either alone.

Murine leprosy was induced in mice with bacilli from animals that had been treated with B.663 and isoniazid in combination for 816 days. The newly infected mice were then treated with one or other of the drugs. The preconditioning of the *Myco. lepraemurium* by the combined drugs appeared to prevent the development of resistance to B.663, and to cause a marked delay in the case of isoniazid. The extent of skin pigmentation due to the accumulation of B.663 in tissue was reduced somewhat by concurrent treatment with isoniazid, which suggested that isoniazid had mobilized the stored B.663.

D. S. Ridley.

The following 6 abstracts are reprinted, with permission, from *Trop. Dis. Bull.*, 1966, **63**, 12 :

11. **Application de l'immunofluorescence sur bacille de Stefansky au diagnostic sérologique de la lèpre humaine** (Stefansky's Bacillus (*Mycobacterium lepraemurium*) in the Immunofluorescence Test for the Diagnosis of Leprosy) by F. P. Merklen and F. Cottenot. *Bull. Soc. Path. Exot.* 1965 May-June **58** 3, 332-5.

Mycobacterium lepraemurium was used as antigen for the indirect immuno-fluorescence test with sera of leprosy patients. Fourteen patients with leprosy of the lepromatous type, with bacilli in their nasal mucus, many of them untreated, all gave positive titres of

1/1,024 or higher; sera from patients with tuberculoid leprosy gave titres of 1/512. Twenty-five healthy persons who were tuberculin negative, gaves titres up to 1/16 (but patients with other diseases such as tuberculosis appear not to have been investigated). However, titres of 1/128 or higher are thought to be of diagnostic value in leprosy.

D. S. Ridley.

12. **The Indirect Basophil Test in Erythema Nodosum Leprosum. Preliminary Note,** by S. L. Moschella, W. R. Bell and J. R. Trautman. *Inter. J. Lepr.*, Wash., 1966, Jan.-Mar., **34**, 1, 39-41.

'In this brief and preliminary study, the authors were unable to duplicate the work of Gokhale and Joglekar (*Indian Pract.*, 1964, v. 17, 377) who reported that lepra reactions caused by dapsone could be differentiated from those that occur spontaneously by using the indirect basophil degranulation test. Because of the reasons presented in the discussion, the authors are unable to speculate on the presence or absence of circulating antibodies to dapsone in this study.'

13. **O tratamento das lesões ùlcero-cutnâeas da lepra pelo Vasculat** (The Treatment of Ulcero-Cutaneous Lesions of Leprosy with Vasculat), by J. M. Santos and J. G. De Azevedo. *Rev. Brasileira Med.*, Rio de Janeiro, 1965, July, **22**, 7, 422-7, 27 coloured figs. on 8 pls.

In the many mutilating lesions of leprosy, a broad section are referred to as ulcero-cutaneous, and leprosy can hardly appear as a morbid entity without being associated with other morbid entities which also produce ulcero-cutaneous lesions. Having obtained satisfactory results with Vasculat in non-leprous ulcero-cutaneous lesions, the authors studied results in patients having ulcero-cutaneous lesions in leprosy.

Male and female adults were selected of any state and age, who had suffered from leprosy for some time and had ulcero-cutaneous lesions fairly old and advanced. The patients were in rather a serious condition, so that if a positive result were obtained it could not possibly be attributed to any other medication.

Vasculat was used as tablets: injections were not suitable. The daily dose was 0.075 gm. or 6 tablets (1 tablet of 0.0125 gm. was given every 4 hours). Some patients were receiving treatment with sulphones.

There were 16 patients with bacillary or non-bacillary lesions treated in Brazilian leprosaria for up to 2 months. The paper gives detailed case notes of 8 patients and 27 coloured illustrations. The authors were able to make certain conclusions from their findings:—(1) Vasculat shows itself useful and efficient in the treatment of ulcero-cutaneous lesions of patients with leprosy even when the patients were subject to vascular lesions (varices) or dermatological lesions of other nature (such as eczemas); (2) when auxiliary therapy was not given the therapeutic effects obtained were considered to be entirely due to Vasculat and were of real value; (3) because of these results in the preliminary stage, further investigations on this treatment are called for, together with its possibilities in relation to surgical, antibacterial and other measures.

J. R. Innes.

14. **Primeros resultados del tratamiento de las leprorreacciones con talidomida** (First Results of the Treatment of Lepra Reactions with Thalidomide), by J. Terencio de Las Aguas, and F. Contreras Dueñas. *Rev. Fontilles.*, Alicante, 1966, Jan.-June, **6**, 5, 449-55, 6 figs.

At Fontilles, Spain, the authors treated 6 patients suffering from lepromatous leprosy, 2 men and 4 women, who had also suffered from lepra reactions over several years. Thalidomide was used in an initial maximum dosage of 100 mgm. decreasing slowly to 50 and 25 mgm. and there was improvement in 4 patients. The lepra reaction disappeared in 5 patients, but in 1 patient the treatment had to be suspended after several days because of an allergic incident. The authors say that thalidomide showed its efficacy, and caused a rapid disappearance of the reactional phases in 5 of the patients. The dosage employed was lower than that of Sheskin (this *Bulletin*, 1966, v. 63, 285), but did not surpass 100 mgm. With thalidomide the disappearance of the fever was attained in between 2 and 11 days, with parallel improvement of the cutaneous lesions and above all without the need to continue steroid treatment.

Tolerance was excellent except for 2 patients who had very intense somnolence. The authors believe that thalidomide needs a fuller investigation. (The authors do not explain, or discuss, why this drug is used on females, nor do they discuss its teratogenic properties.)

J. R. Innes.

15. **Effect of Diaminodiphenyl Sulphone and ICRC Bacilli on Acid Phosphatase of Macrophages,** by K. Prabhakaran and C. V. Bapat. *Indian J. Med. Res.*, 1966, May, **54**, 5, 458-61.

Mouse intraperitoneal macrophages showed an increase of 30% in acid-phosphatase activity when incubated *in vitro* or *in vivo* with DDS. The increase was greater in the case of aged cells. It is suggested that DDS may produce lysis of *Mycobacterium leprae* indirectly by causing the release of lysozymes in the host cells.

Incubation of macrophages with ICRC bacilli affected their acid phosphatase activity in much the same way as did DDS.

D. S. Ridley.

16. **Enhanced Susceptibility of Thymectomized and Irradiated Mice to Infection with** *Mycobacterium leprae*, by R. J. W. Rees (Correspondence). *Nature*, 1966, Aug. 6, **211**, 657-8, 1 fig. (15 refs.).

The possibility that thymectomy and X-irradiation of mice would enhance the multiplication of *Mycobacterium leprae* in footpads was tested in 24 animals. Twelve were thymectomized when 2 months old and 16 days later were exposed to 900r and then given a transfusion of marrow; the remaining 12 animals were kept as controls. Four weeks later all animals were

inoculated with 10^4 bacilli. In one experiment the *Myco. leprae* were obtained direct from man and in a second experiment a first passage strain from mice was used. In both experiments the infections were enhanced in the thymectomized irradiated animals, the yield of bacilli being about 10 times greater in the first experiment and a 100 times in the second. But there was no systemic spread of the infection. It is likely that the limitation of infection to the footpad (mainly in muscle fibres) is due partly to an immunological factor but it is not clear whether this is the only factor.

D. S. Ridley.

The following 7 abstracts are reprinted, with permission from *Trop. Dis. Bull.*, 1967, **64**, 1 :

17. **Some Facts about Leprosy—Guide for Social Camps,** by DHARMENDRA. *Leprosy in India*, 1966, Jan., **38**, 1, 18-35, 20 figs.

This article contains clinical photographs, maps, and clinical studies of several aspects of leprosy including eye involvement, and should be intimately studied. Although it is about leprosy in India, it will be of value to all.

(The article is published as a booklet suitable for the use of village workers, teachers, and social workers. It may be obtained from the Director, Central Leprosy Institute, Chingleput, Madras, price 50 paise.)

J. R. Innes.

18. **Sensitivity of *Mycobacterium leprae* to Low Levels of 4,4″-Diaminodiphenyl Sulfone,** by C. C. SHEPARD, D. H. MCRAE and J. A. HABAS. *Proc. Soc. Exper. Biol. & Med.*, 1966, July, **122**, 3, 893-6 (16 refs.).

Multiplication of *Mycobacterium leprae* in mice was completely inhibited by DDS in concentrations as low as 0.00001% of the diet, which is equivalent to 10 μgm./kgm./day. It is only a 100th part of the lowest dose that produced detectable levels of DDS in the blood, and the tissue level achieved by it is about 1,000th of that produced by a therapeutic dose of DDS in man. There was no evidence of concentration of the drug at the site of infection.
(See also this Bulletin 1965, v. 62, 535.)

D. S. Ridley.

19. **A Study of the Transmission of Leprosy in Families,** by E. B. CHRISTIAN, A. SHAMRAO, L. R. CHRISTIAN, J. J. CHRISTIAN and I. V. CHRISTIAN. *Leprosy in India*, 1966, Jan., **38**, 1, 9-17.

The authors studied 793 families in Zaheerabad in India and found that the most favourable condition for the transmission of leprosy in families existed where there was a close, intimate and prolonged contact with a patient suffering from lepromatous leprosy, whether a parent or close relation. Children in close or casual contact with persons with other forms of leprosy are rarely infected, and when such infection occurs it may result from a temporary 'open' stage of the disease, or to contact with a person with an 'open' infection outside the family.

In the present study the infection usually took place in childhood. Leprosy sometimes developed in children in families in which neither the parents nor grandparents were affected. In the children the incidence of the lepromatous type was much higher (14%) than that of the non-lepromatous (9%).

Although the patients with lepromatous leprosy are the most serious source of infection, only about 30% of the children exposed to them in the family get the disease, the remaining 70% escape. This confirms the view that leprosy is only feebly infective, and that infection with *Mycobacterium leprae* is but one of the factors in the transmission of the disease. The factor of immunity calls for study and in this connexion attention is drawn to the infrequency of conjugal infection, and to the rarity of infection among the staff of leprosy hospitals, and their families.

J. R. Innes.

20. **A propos de la valeur immunologique de la réaction de Mitsuda** (On the Immunological Significance of the Lepromin Test), by J. COUDERT, A. BASSET, J. ROUSSET, R. PRADINAUD and LU-HUYNH-THANH. *Bull. Soc. Path. Exot.*, 1965, Mar.-Apr., **58**, 2, 132-40.

The authors cover familiar territory in their findings on the lepromin reaction in patients suffering from lepromatous or tuberculoid leprosy and in contacts, in Africa and Europe, but break comparactively new ground in reporting 2 histologically distinct types of late (or Mitsuda) reaction in patients with lepromatous leprosy. Basing their study on 286 patients in all, they found that intradermal inoculation with various antigens (*Mycobacterium marianum*, BCG and tuberculoid) gave a variably high proportion of positive results, both early and late, in patients with lepromatous leprosy.

About two-thirds of patients who had been treated with a vaccine prepared from killed *Myco. marianum* gave early and late reactions when tested with antigen prepared from *Myco. marianum*, whether they had lepromatous or tuberculoid leprosy. There was incomplete concordance between the early and late reactions. Histological examination of the inoculation sites disclosed 2 distinct types of reaction—typically lepromatous (except for the absence of bacilli) and typically tuberculoid.

The authors conclude that the Mitsuda reaction is a useful investigative tool for ascertaining the degree of tissue resistance shown by patients with tuberculoid leprosy, and for indicating the occurrence of non-susceptibility to leprosy in contacts, but cannot indicate the underlying immunological state of the individual.

It is suggested that the generally recognized anergy of lepromatous leprosy is a concept that should be restricted to patients with leprosy infections of the lepromatous type, and that some signs of hyperergy may appear after injection of an antigen prepared from related mycobacteria.

(This paper incidentally emphasizes the need for some internally accepted standards of preparation and antigenic activity of lepromin as used widely for testing.)

S. G. Browne.

21. **Smallpox Vaccination and Acute Exacerbation of Leprosy,** by K. RAMANUJAM and G. RAMU. *Leprosy in India*, 1966, Jan., **38**, 1, 3-9, 2 figs.

The authors, and others, have found that vaccination against smallpox among persons suffering from leprosy seems to be a definite provocative factor for the precipitation of acute exacerbation of the disease, especially in patients with lepromatous leprosy (this *Bulletin*, 1935, v. 32, 347; 1941, v. 38, 222; 1954, v. 51, 275; 1963, v. 60, 132). Of 567 patients with lepromatous leprosy, 100 (17.6%) developed an acute exacerbation of the disease after vaccination, and in 48 of these 100 patients it was the first exacerbation. It was the authors' experience that such an exacerbation may be the first of several similar episodes. A direct relationship was found between the intensity of local reaction to vaccination and the chances of occurrence and severity of the acute exacerbation of leprosy. The treatment of the acute exacerbation after vaccination is very much the same as for that arising spontaneously, or from other causes; the authors suggest antibiotics could be used with advantage as there is local pustulation and lymphadenopathy. Patients in leprosaria should be revaccinated periodically which would perhaps ensure less severe local reaction to vaccination and thereby reduce the incidence of acute exacerbation of leprosy.

J. R. Innes.

22 **An Interesting Reaction in Leprosy,** by J. C. TILLEY. *Southern Med. J.*, 1966, July, **59**, 7, 766-8, 4 figs.

The author draws attention to an interesting reaction which may occur in leprosy when the skin is frozen. The reaction depends on cryoproteins present in patients suffering from leprosy and the case histories are given of 2 patients in the leprosarium at Carville, Louisiana. The lesions, which are produced by freezing the skin with ethyl chloride, are very unusual. Four figures are given and these show their peculiar nodose type and their association with ulceration. MATTHEWS and TRAUTMAN have demonstrated the presence of a cryoprotein and have shown that 89% of the patients with lepromatous leprosy had cryoproteinemia and so did all of 6 patients with dimorphous leprosy, whereas in tuberculoid leprosy cryoproteins were absent. When leprosy became inactive there were no demonstrable cryoproteins. Further studies are in progress.

(See also this *Bulletin*, 1966, v. 63, 284.)

J. R. Innes.

23. **Lisozima no tratamento de doentes de lepra em manifestação aguda** (Lysozyme in the Treatment of Leprosy Patients with Acute Manifestations), by L. C. PEREIRA. *Publicações Centro, Estudos Leprológicos*, Curitiba, 1965, Nov., **5**, 2, 71-80. English summary.

The author treated 7 patients suffering from the lepromatous form of reaction and 1 with tuberculoid reaction, using lysozyme (Laboratil Lisozyma). He obtained excellent results in acute forms of reaction and found that it worked well with adjuvant cortisone. It allowed a smaller dosage of cortisone and so reduced the side-effects. The daily dose was 150 mgm. intramuscularly and orally for between 13 and 60 days, and the observation period lasted 120 days. Details are given of each of the 8 patients treated.

J. R. Innes.

The following 8 abstracts are reprinted, with permission, from *Trop. Dis. Bull.*, 1967, **64**, 2 :

24. **The Leprosy Problem in the World,** by L. M. BECHELLI and V. M. DOMINGUEZ. *Bull. World Health Organisation.* Geneva. 1966, **34**, 6, 811-26, 1 map on folding pl. (23 refs).

The authors, in an attempt to provide realistic figures, find there is a lack of accurate data on the prevalence of leprosy in the different countries of the world because case-finding has not reached a high level in many countries. In all there are 2,831,775 registered patients and 10,786,000 estimated patients, though this figure may well be an underestimate. The number of patients under treatment is about 2,000,000, about 68% of the registered patients and 18% of the estimated. About 2,097 million people live in areas with prevalence rates of 0.5 per thousand or higher; in these areas nearly one million new leprosy patients can be expected in the next 5 years. The estimated number of disabled patients is 3,872,000.

A useful table, which occupies 9 pages, shows for each country in the world the estimated number of patients and the number registered and treated, together with the date and source of information, though this information is not complete in every instance.

J. R. Innes.

25. **A Culture Medium for the Isolation of Acid-fast Bacteria in Leprous Materials,** by M. C. MABALAY and E. B. MABALAY. *J. Philippine Med. Ass.*, 1966, Apr., **42**, 4, 195-211. (21 refs.)

The authors claim that by using a special medium they have grown mycobacteria from lepromatous lesions of each of 109 patients at the Eversley Child Sanatorium, Cebu, in the Philippines. This medium consisted of a liquid base containing 5 gm. $NaHPO_4$, 1.5 gm. KH_2PO_4, 0.6 gm. $MgSO_4$, 2.5 gm. Na citrate, 5 gm. asparagine, 50 ml. glycerol per litre to which was added, after sterilization, 10-20 gm. of rice flour which had been heated to boiling point until the flour

was cooked and 2 ml. of a 1% alcoholic solution of gentian violet per litre. It was distributed in quantities of 2 ml. and autoclaved at 15 lb. pressure for 30 minutes. At the time of inoculation an equal volume of a mixture of equal parts of the liquid base and bovine serum, which had been sterilized by membrane filtration, was added to the medium. The pathological material consisted of skin biopsy specimens, blood, urine, nasal washings, sputum, skin and ear lobe scrapings, purulent material from ENL lesions and pus from a lung abscess. Some portions of these were treated with 4% sodium hydroxide for 1 hour and immediately neutralized with normal hydrochloric acid before inoculation into the medium (see TERNI and SIGNORINI, this *Bulletin*, 1951, **48**, 266).

Mycobacteria grew from the biopsy material, and from the specimens of pus, which had not received treatment with sodium hydroxide, in a mean incubation period of 111.3 days and 212.2 days, respectively, but from the treated samples the respective times were only 29.3 days and 13.0 days. The first sign of growth in the liquid medium was a change in colour of the gentian violet and later there was pellicle formation. When subcultured on to a solid medium consisting of the fluid isolation medium and whole egg, the organisms produced a bright canary yellow to deep orange pigment. They grew as moist or slimy colonies tending to coalesce or form aggroupments at the sites of inoculation with little or no tendency to spread outside the line of seeding. Microscopically the organisms varied from short, solidly-staining, moderately acid-fast bacilli to long, slender, sometimes beaded, rods. After a few weeks the shorter forms were invariably observed to elongate and become beaded; occasionally globi-like formations were seen.

Intradermal inoculation of the slender rod form into patients suffering from lepromatous leprosy provoked a Mitsuda-type of reaction which sometimes ulcerated, but the shorter strains behaved similarly to regular lepromin in patients with tuberculoid leprosy and in those with the lepromatous form.

The authors also claim to have produced slow but perceptible growth of *Mycobacterium lepraemurium* in this medium. Other mycobacteria, namely *Myco. tuberculosis*, *Myco. phlei* and the Binford bacillus, grew uninhibitedly in the medium.

The authors consider that their success is due in part to the medium, but mainly to the treatment with sodium hydroxide. This process renders the resistant bacilliary membrane permeable so that the bacillus becomes exposed to the nutrients in the media and, in the absence of host tissue cells, the organisms rapidly adapt themselves to their new environment. (In a footnote, the authors state that the strains have been examined by Dr. R. J. W. Rees of the National Institute of Medical Research, London, and that he considers that they belong to the Runyon III group of atypical or unidentified mycobacteria.)

S. R. M. Bushby.

26. **Demonstration of *Mycobacterium leprae* in Tissue. Demonstration by means of Khanolkar's Concentration Test followed by Fluorescent Staining.** by W. A. AKERS and W. C. MORSE. *Arch. Dermat.*, 1966, Sept., **94**, 3, 361-2.

Mycobacterium leprae was demonstrated in human skin by fluorescent staining, after concentration by Khanolkar's technique (this *Bulletin*, 1952, **49**, 1048), when it could not be demonstrated by the usual histological methods. The patient had tuberculoid leprosy and his routine sections were consistently negative. After concentration, bacilli could be found by means of Ziehl-Neelsen's method, but much better results were obtained with auramine O and rhodamine D fluorescent staining. For details of technique the reader should refer to the original paper.

D. S. Ridley.

27. **Miositis lepromatosa** (Lepromatous Myositis). by A. ODERIZ, O. REYES and J. CONVIT. *Dermatología Venezolana*, 1965, Dec.—1966, July, **5**, 1/2, 50-55, 3 figs.

The English summary appended to the paper is as follows:

'The authors described a case of lepromatous leprosy with reactional lesions in an adult male who had not received specific treatment. The patient shows infiltration of the muscular masses of the arms and legs. Biopsies taken from those lesions reveal lepromatous granulomata in the muscular interstices and a degenerative process of the muscular fibres with deteriorated acid-fast bacilli. Special dyes were used for a better study of the case. A review of the literature is made and comments on the frequency, age, sex, etc., of the patients published so far.'

(See also this *Bulletin*, 1960, **57**, 713; 1961, **58**, 1020.)

28. **Dapsone-Resistant Lepromatous Leprosy in England,** by A. R. D. ADAMS and M. F. R. WATERS. (Memoranda.) *Brit. Med. J.*, 1966, Oct., **8**, 872.

This is an account of the first patient in England suffering from leprosy, who has been proved resistant to treatment with dapsone. The authors used techniques described by PETTIT and REES (this *Bulletin*, 1965, **62**, 108) in Malaya. They made a suspension of *Mycobacterium leprae* from biopsy material and inoculated 36 mice with approximately 10,000 bacilli in the pad of each hind foot. The animals were then divided into 6 groups; one group acted as an untreated control group, and the other 5 groups each received one of the following drugs mixed in their diet: 0.1% dapsone, 0.025% dapsone, 0.1% thiambutosine, 0.2% thiacetazone, and 0.1% sulphadimethoxine. The mice were killed after 5 to 9 months. Limited multiplication of *Myco. leprae* was detected in the footpads of both the control animals and also of the animals fed with dapsone. The infection was completely suppressed by thiambutosine and thiacetazone, but only partly suppressed by sulphadimethoxine.

The patient was well on arrival in England from Bengal but 2 years later developed lesions of lepromatous leprosy. He had received treatment with sulphone 15 years previously at a leprosarium in India.

This account should be carefully studied in the original. The resistance to dapsone may be connected with irregular treatment.

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29. **Management of Uncomplicated Plantar Ulcers in the Field,** by S. M. MUKHERJEE. *Leprosy in India*, 1966, April, **38**, 2, 107-15, 2 figs.

'The problem of plantar ulcer still remains unsolved. The important role of para-medical personnel in solving this problem has been discussed. He can and should deal with the early and uncomplicated ulcers. The two main things necessary for this are: (i) to protect the ulcer from injury and infection by means of antiseptic dressings, and (ii) to put the foot to rest by means of a plaster-of-paris cast. Details are given of these two procedures.

'Treatment of complicated plantar ulcer has not been described, as patients with complicated ulcers should be treated by the medical personnel.'

30. **An Epidemiologist's View of Leprosy,** by K. W. NEWELL. *Bull. World Health Organization*, Geneva, 1966, **34**, 6, 827-57. (Numerous refs.)

While leprosy has been studied exhaustively by leprologists, it is only recently that persons in other disciplines have given it the attention it deserves. The author reaches the conclusion that the anergic, or factor N, hypothesis (ROTBERG, this *Bulletin*, 1958, **55**, 50; DOULL, *ibid*, 1962, **59**, 981) evolved to relate the lepromin test to the findings in clinical leprosy is most promising, and if this should be proved to be correct, he thinks it unlikely that BCG vaccination can be a very useful tool in the prevention of leprosy. The argument, and the very full review and discussion can be appreciated only in the original

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31. **Rehabilitation Project at Purulia Leprosy Home and Hospital,** by J. PITTS. *Leprosy in India*, 1966, Jan., **38**, 1, 43-8. (Reprinted from *J. Rehabilitation in Asia*, 1965, Oct., **6**, 4.)

The author in making a study of rehabilitation at Purulia Leprosy Home and Hospital, India, has decided on 3 ways in which help may be given to patients: (1) by close contact with their homes and families by regular periods away from the hospital at home as well as help from the welfare officer; (2) by learning a skill or trade so that, when discharged, the patient can support himself; (3) by providing industrial work at the leprosarium and later in village centres linked with the leprosarium or perhaps later with government rehabilitation schemes. The paper is practical and worthy of study in the original.

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