REVIEWS

International Journal of Leprosy, Vol. 22, No. 4 (Oct.-Dec. 1954).

In the Editorial, Wade traces the slow growth of the idea of the " borderline " as a special type of leprosy. He gives two points mentioned in recent articles which seem worth mentioning:—

" (1) From the experience of many workers in the period when various dyes were being tried out in leprosy therapy, it is known that after repeated intravenous injection of methylene blue in lepromatous cases the skin lesions became coloured, so that even ' inapparent ' lesions are made evident, because of selective absorption of the dye by the lepra cells. On the other hand tuberculoid lesions remained uncoloured, the cells which compose them lacking the capacity to store dyes. Montel, in his article in this issue of *The Journal,* tells of cases with both tuberculoid and lepromatous lesions, the former uncoloured by methylene blue, the latter intensely stained by it; and a photograph is presented to demonstrate this condition. This statement suggests a new means for the study of borderline cases, one by which anyone who can give the necessary course of injections might obtain help in differentiating between the severe reactional tuberculoid case that has not gone over and may be expected to subside to the quiescent phase, and the case whose lesions have actually begun to go over the border to the lepromatous region of the spectrum.

" (2) Another point of interest is the recent report of Hale, Molesworth and others on isoniazid treatment. A large proportion of the cases studied were of an ' atypical ' class, ' more or less of the order of what is called " borderline " by some workers.' They stated that erythema nodosum leprosum occurred in many of the lepromatous and atypical cases, especially if the dosage was high. Now, it is generally recognised that that type of reaction is a characteristic of lepromatous cases but not of tuberculoid. That being true, it follows that if a borderline case under

treatment develops this reaction, it has gone pretty far in its essential character to the lepromatous side. It is suggested that observations on this point should be recorded."

" Clinical Evaluation Studies in Lepromatous Leprosy," by J. A. Doull. An acount is given of a carefully planned evaluation of the treatment of leprosy made in four widely-separated institutions: Aisei and Komyo in Japan, Eversley Childs Sanatorium in the Philippines, and the Westfort Institution near Pretoria in South Africa. The following drugs were used either alone or in combination: Diasone, DDS, dihydrostreptomycin and PAS. The patients were suffering from lepromatous leprosy and were arranged in comparable groups. Control groups were arranged with PAS at Westfort, and with placebos at the other institutions. The trials took place for 32 to 48 weeks. The results were judged on clinical findings such as changes in infiltration and nodules and the healing of ulcers. Bacteriological changes were judged by comparisons of smears from five or six sites made before and after the periods of treatment. Lepromin tests were also done in all the patients.

All the drugs were beneficial in approximately the same degrees. From 0.5 to 0.3 improvement was shown in the various groups. Combinations of drugs did not add to the effectiveness. One-sixth part of those on PAS showed improvement, and there were some improvements even among those on placebos. Bacteriological results changed to negative in a few in each group, even in the controls. It varied from 5.3 to 23.3 per cent. In a few patients the lepromin test changed from negative to doubtful or positive. (See Editorial on page 139.)

Guinto, R.S., Rodriguez, J. N., Doull, J. A. and De Guia, L., write on " The Trend of Leprosy in Cordova and Talisay, Cebu Province, Philippines." This is probably the most thorough and concentrated piece of epidemiological research on record. The Municipality of Cordova was surveyed for leprosy in 1933 and 1941, and re-surveyed in 1950-51. Combining the results in these two areas, the earlier surveys gave 19.3 per thousand, and the later ones fourteen years later 18.5 per thousand. Although lepromatous leprosy had diminished from 11.6 to 5.4 per thousand, the non-lepromatous forms had increased from 7.7 to 13.1 per thousand. These changes had occurred equally in both municipalities and in both sexes. The increase in the non-lepromatous forms was most marked in children. The yearly incidence for males with the lepromatous form was 0.39 per thousand, and for females 0.25; with the non-lepromatous forms it was 0.82 for males

and 0.67 for females. The total yearly incidence was 0.75 cases per thousand, the maximum being in the 10-14 age group. The diminution of lepromatous leprosy was less pronounced in those who had been subjected to home infection as compared with those who had not been so exposed. The change over to the less severe forms, if maintained, would suggest that a gradual eradication of the disease is taking place.

Hanks, J.H., describes the "Relationship between the Metabolic Capacity and the Infectiousness of M. leprae murium." This is one of a series of articles by the same author in which the relationship of the metabolism of mycobacteria, and particularly of the bacillus of rat leprosy, to their infectiousness is studied. The two methods of measuring the metabolic activity are the respiration and the hydrogen transfer capacity (HTC) of the mycobacteria. While metabolic study may provide new insight into pathogenesis, the simultaneous inoculation of animals appears necessary in order to learn the "basic ground rules." When these rules have been fully learned, metabolic study will be able to replace the tedious and expensive observations in animals. The animals must, however, always be kept "as a court of final appeal."

It was found that although at room termperature the HTC and the infectiousness of Myco. leprae murium deteriorated rapidly, washed organisms could be kept in a refrigerator from deteriorating for a fairly long time in a suspension of sucrose solution with pH 7.5. Still better results were obtained with albumen and yeast supplement added to the solution.

Hanks, J. H. and Gray, C. T., write on "Extracellular Inhibitors in Leprotic Infections and their Role as Barriers to Experimental Transmission." The hydrogen transfer capacity test and inoculation in rats showed that Myco. leprae murium was adversely affected as regards its endogenous metabolism and viability by exposure to serum taken from rats and other animals. It is considered that possibly this process accounts in a similar way for the difficulty in transmitting human leprosy. In the case of Myco. leprae murium protection against such damage to the organisms may be obtained by prolonged refrigeration in albumin solutions.

Leprosy in India, Vol. 27, No. 2, (April 1955).

This issue is devoted entirely to the All India Leprosy Workers' Conference, held in Jamshedpur on March 5th and 6th, 1955, and

to the Second Biennial Meeting of the Indian Association of Leprologists which met on the two previous days.

In the opening address the President mentioned that the new Central Leprosy Teaching and Research Institute in Madras will doubtless make its own contribution in due course in all aspects of the leprosy problem. Mr. Nehru, in a message to the Conference, wrote: " I am glad that this fight against leprosy has been taken up in earnest in India. I wish it every success. I need not point out that we should work for positive health and well-being and not merely to cure illness." Mr. Bailey of the Mission to Lepers got to the root of the problem when he said: " In the absence of . . . suitable personnel, any scheme of work, however intelligent it might be, was bound to be a failure. To overcome this shortage of dedicated individuals and to produce an army of such persons, every worker should make up his mind to win over at least one other individual to this cause."

The Director-General of Health Services, Government of India, made an important speech regarding the future policy of the Government.

" Full advantage has got to be taken of the almost spectacular results of the sulphone therapy in a campaign for the eradication of the disease. For this purpose, it would be essential to establish, both in rural and urban areas, special leprosy clinics in sufficient numbers in order to make the treatment readily available to the patients." He said that two types of control units were envisaged: " treatment units " and " study units." A few pilot units had already been begun, and it was hoped to raise the number to 25. A sum of Rs. 30 lacks (about £225,000) had been allocated for the purpose in the remaining period of the remaining five-years period of the First Five-Year Plan. Each unit would cover a population of about 50,000 persons in known endemic areas. The units had been provided with facilities for the assessment of the results of sulphone therapy, and for the study of yet unsolved problems in the epidemiology of the disease. " A careful watch will be kept on all contacts and they will be brought under treatment whenever necessary. Health visitors will make periodic domiciliary visits to ensure the fulfilment of the above objectives, and health education will form an integral part of the programme. The results will be assessed after another detailed survey after the scheme has been in operation for a certain number of years, and in comparison with a control area where incidence of the disease will be studied but where no special measures will be undertaken apart from the traditional ones normally available in the area." It is also proposed to take up a trial of the value of BCG in association with one of the research units, this being given by mouth and with suitable controls. It is estimated that there are more than a million sufferers from leprosy in the country, while there are only 18,500 beds available and only 1,000 outpatient clinics for treatment. Special stress is to be laid on leprosy in the undergraduate curriculum and on post-graduate training of doctors. It is not proposed to create a special cadre of Medical Leprosy Officers as few would desire to remain as leprosy doctors throughout life. He suggested that it would be better to " create workers with special training in the general field of epidemiology who could then be seconded for dealing with problems as they arise, be they in the field of leprosy or tuberculosis or any other. It is far more desirable to create a multi-purpose doctor than the one

qualified to deal only with one isolated aspect of any medical or public health problem."

Dr. Mukherji said, regarding the planning of BCG trials: " One method of approach seems to be the selection of an endemic area with a more or less static incidence of leprosy, containing a sufficient number of child contacts, dividing the area into two, vaccination being given to one, and the other serving as a control. A better method seems to plan the investigation in a familywise basis, taking the area as a whole, half the number of lepromin-negative contacts in a family being vaccinated and the other half serving as control. It is also important to keep the lepromin-positive contacts in such families under observation at the same time."

In a paper on methods of testing the prophylactic use of DDS in child contacts, Dr. Wardekar said that all the children chosen should be lepromin tested and divided into groups. Lepromin-positive children are divided into two groups, one being given DDS and the other not, the two groups being compared for assessing the results. The lepromin-negative children should be inoculated with BCG and retested with lepromin. Those that become positive should be treated in two groups again as above. Those that persist as negative should be divided into two comparable groups, the one being put on DDS and the other not. If sufficient numbers were tested in this way the results would be of value.

Drs. Dharmendra and K. R. Chatterji read a paper of particular value as it covers a period of 20 years.

There were found available for re-examination in the District of Bankura, 680 patients, the records of whose lepromin tests performed 15 to 20 years previously were available. After these periods of years it was found that of 156 negative reactors 9.6 per cent had developed lepromatous leprosy, and 4.4 per cent non-lepromatous leprosy. Of the 524 positive reactors only 3.2 per cent had developed leprosy, and all these were of the mild non-lepromatous type.

In one of the experiments made 20 years before, an attempt was made to increase the reaction to lepromin by repeated testing, and for this purpose a total of three tests was done in 109 of the lepromin-negative patients in the course of one year. In 93 of these the reaction became positive (weak in 30, moderate in 35, and strong in 28). " It cannot be said to what extent this conversion from negative to positive was a result of the repeated testing; however, since the positive result was seen after the repeated testing, these individuals should be excluded while assessing the value of a spontaneous lepromin reaction. Their exclusion will reduce the number of negative reactors to 63, while the number of positive reactors will remain unchanged (524)." A correlation of the results of the lepromin test on there 587 persons with the development of leprosy and type of disease shows that of the 63 negative reactors 22.2 per cent developed lepromatous leprosy, and 4.7 per cent non-lepromatous. These findings point to the great prognostic value of the lepromin reaction in persons exposed to leprous infection. They lend support to the generally

held view that compared to the contacts who have a positive lepromin reaction, those who have a negative one are likely both to develop the disease and get it in the more serious form.

A paper by Dr. Paul Brand of the Christian Medical College, Vellore, is of outstanding interest and value. Especially encouraging is the hope he gives of remedying one of the most distressing disabilities of leprosy—drop foot. He describes briefly his technique:

> "Even as the median nerve is spared in the upper arm when the ulnar and radial may be paralysed, so in the leg the medial popliteal nerve is preserved when the lateral popliteal and posterior tibial are lost. It does not become paralysed until it has given off its branches to the gastrocnemius, soleus and tibialis posterior. This means that the tibialis posterior muscle is available for a tendon transplant operation for the correction of drop-foot. If this operation is planned, it is essential that all foot ulcerations should be soundly healed before tendon surgery is attempted. The tibialis posterior is then detached from its insertion and re-routed subcutaneously from the middle of the calf across the front of the ankle joint and inserted into the middle cuneiform bone. This operation has only been introduced recently for leprosy patients, and we are still following up the early cases. It is safe to say even at this stage that the results are encouraging and that the operation may be recommended for further trial."

The Conference was attended by 160 medical and non-medical delegates, and was held in Jamshedpur, India's great industrial city.

Drs. Ramos, Silva and Peryassu write on "Some Observations on the Treatment of Leprosy, particularly the Tuberculoid type, with Streptomycin, alone or in combination with Sulphones" (Brasil-Médico, 1954, Vol. 68, p. 439). They first refer to former work on this subject and then describe their own experiences. They treated 27 patients for periods up to 3½ years, 20 being for more than a year. With the exception of one indeterminate case all were of the tuberculoid type. The dosage was 1 gm. of dihydrostreptomycin injected once or twice daily intramuscularly. The minimum total dose was 80 gm. and the maximum 180 gm. Of the 27 patients 26 showed a disappearance of all active signs. Lesions became flattened and lost their erythema. Nerves lost their thickening almost entirely and there was a considerable restoration of sensation. Histologically, there was quick change in the tuberculoid granuloma with a change of the epithelioid cells into vacuolated cells resembling those of Virchow. Later, lymphocytic infiltration alone remained, and this also gradually disappeared.

In addition to streptomycin, sulphone treatment was given later for fear that bacilli set free by the former drug might form fresh lesions. The authors, however, consider that the good results were due chiefly to streptomycin. In only one patient was there

a relapse, with an outbreak of tuberculoid reaction occurring five months after all the lesions had apparently cleared up.

Drs. Perrin and Caplin (Arch. Dermat. 1955 (June), 71, p. 742) write on "Leprosy Acquired during World War II." This is only the second case of leprosy that has been reported among the U.S. forces so far, apart from two patients in whom leprosy developed in tatoo marks. The present patient is a negro who worked in the navy, but was employed during the war in rounding up patients with leprosy in the Philippines. Although from the photographs and from the bacteriological examination this appears as a very obvious case of the lepromatous type, there was considerable difficulty and delay in making a diagnosis, showing how necessary was Levan's comment to be watchful for leprosy in veterans of World War II and the Korean campaign who have served in endemic areas.

Drs. Nakawa and Nakamura, writing in the Kurume Medical Journal (1954, Vol. —, p. 135), describe their method of keeping rat leprosy bacilli alive for at least 2½ years. They made a suspension of rat leprosy leproma, and after diluting it five times, added equal quantities of various solutions: saline, saline with inactivated bovine serum, 4 per cent glycerine water, and 10 per cent Kirchner's medium. These dilutions were placed in 1 c.c. ampoules, frozen and evaporated with a rotary pump. They were examined after 7 months and again after 2½ years. While the first two suspensions were found to be in the form of a dry powder, the other two, especially the one with glycerine, were not dry. When rediluted and injected into rats, all of them showed live and infective rat leprosy bacilli, but greater infectivity was shown by the suspensions that had been completely dry, especially the one diluted with bovine serum.

Drs. Laviron and Kerbastard write in the Bulletin Soc. Path. Exot. (1953, Vol. 48, p. 129) that after seeing the published work of Lemaire and Housset in the treatment of vascular and trophic affections with intravenous injections of bile salts, they used similar injections of sodium dihydrocholate in 11 leprosy patients suffering from perforating ulcers and other leprosy ulcers, some of which were of up to 3 years' duration. Five perforating ulcers of 6 months' to 2 years' duration healed up rapidly. Eight others, some of them very bad and of long duration, were very much improved. In only one case did the improvement, rapid at first, not continue.

A 20 per cent solution is used and 5 to 10 c.c. injected intravenously, very slowly, daily for 15 to 20 days. In no case were there any bad results, though there is a bitter taste in the mouth and may be a feeling of nausia for about ten minutes. The results obtained justify further trial of this method.